DISEASES of the CHEST

VOLUME XXXVII JUNE, 1960 NUMBER 6

Effect of Atropine on the Pulmonary Circulation During Rest and Exercise in Patients with Chronic Airway Obstruction*

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Abbott and co-workers[1] have reported that atropine reduced pulmonary hypertension in patients with pulmonary emphysema. This effect was particularly evident during muscular exercise. Patients with so-called "fixed" emphysema did not respond to this medication, whereas patients with other forms of emphysema did. The present investigation was designed to investigate further the effect of vagal block by atropine on pulmonary hemodynamics during rest and exercise in patients with pulmonary hypertension secondary to chronic asthma or emphysema.

Materials and Methods

Twelve patients with asthma or emphysema who had been evaluated repeatedly in the Cardiorespiratory Laboratory at Grasslands Hospital were selected for the present study. Previous evaluation included: A. Spirometry, with calculation of maximal mid-expiratory flow rate (MMF)[2] and vital capacity, B. One or more measurements of arterial blood gas composition by the Van Slyke manometric technique with calculation of arterial carbon dioxide tension ($P_{A_{CO_2}}$) from the arterial blood pH, C. Measurement of the diffusing capacity of the lung (D_{CO}) during rest and exercise by the steady state carbon monoxide method developed by Filley and co-workers[3] and D. Calculation of the ratio of lung dead space to tidal volume (V_D/V_T) from analysis of expired air and arterial blood carbon dioxide tension.[4]

Right heart catheterization was performed under basal conditions, with measurement of pulmonary artery or right ventricular pressure by a Statham strain gauge on an Electronics for Medicine Research Recorder. Mean pressures were measured by electronic integration of the pressure pulses. Cardiac output was calculated using the Fick formula, from analysis of expired gas composition and volume, and arterial and venous oxygen content. Total pulmonary resistance to blood flow, expressed as mm. Hg./1./min., was calculated by dividing the mean

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Aided by grants from the Westchester Heart Association and Westchester Tuberculosis and Public Health Association.

TABLE 1 — HEMODYNAMIC STUDIES BEFORE AND AFTER ADMINISTRATION OF ATROPINE

Patient	State		Pulm. Art. Pr. mm. Hg. Sys	Dias	Mean	Heart Rate	Cardiac Index l./min/M²	Oxygen Cons. CC/min STPD	Art. O_2 Sat. per cent	Aver. Resp. Variation Sys. Pr. mm. Hg.	Total Pulm. Resis. mm.Hg/ l./min.
Normal											
	Rest		25	12	16		3.0		97		3.0
No Response											
L. O.	Rest	a	26	11	19	78	3.47	257	88	15	3.22
		p	27	11	17	84				11	
	Ex.	a	54	41	46	114	6.22	771	89	17	4.35
		p	44	36	41	129	5.69	768	90	14	4.24
J. B.	Rest	a	27	13	16	84	3.23	217	90	7	3.06
		p	25	13	15	108	3.31	298	89	9	2.80
	Ex.	a	46	20	36	114				14	
		p	38	24	28	132				17	
F. Me.	Rest	a	39	19	26	78	3.63	211	89	21	5.20
		p	28	16	21	96				8	
	Ex.	a	51	24	35	90	3.66	316	89	36	6.93
		p	41	20	32	102	3.06	277	88	30	7.59
J. S.	Rest	a	49	16	24	72	3.15	236	85	16	4.28
		p	36	13	26	86	2.89	233	85	14	5.05
F. Mo.	Rest	a	55*			39	2.01	211	89	20	
		p	61			38	2.15	219	87	13	
E. M.	Rest	a	26	7	14	66	2.15	219	82	15	3.61
		p	35	15	22	84				13	
	Ex.	a	46	25	37	86	3.74	600	82	21	5.50
		p	56	21	38	120	3.80	719	86		5.56
M. C.	Rest	a	35	16	22	90	2.36	250	85	21	5.01
		p	38	18	26	120	2.64	264	86	23	5.30
L. M.	Rest	a	33	13	21	93	2.03	263	81	24	6.05
		p	33	16	22	102	1.92	248	81	23	6.70
	Ex.	a	61	26	38	102	3.62	448	69	28	6.13
		p	46	21	30	108	2.77	423	79	28	6.34
Fair Response											
G. W.	Rest	a	34	7	16	105	3.56	223	90	6	3.21
		p	33	10	16	145				7	
	Ex.	a	44	15	22	136	4.62	463	87	12	3.40
		p	38	13	21	162	5.56	488	85	10	2.69
J. C.	Ex.	a	25	17	22	120	3.07	490	90	14	4.56
		p	21	10	16	120	4.12	573	87	6	2.47
K. P.	Rest	a	30	8	15	70	1.99	172	94	14	4.60
		p	22	8	15	108	2.66	209	92	3	3.43
	Ex.	a	56	19	32	114	4.03	615	95	23	4.85
		p	30	13	22	136	3.85	548	94	9	3.48
Good Response											
T. M.	Rest	a	63	35	46	114	2.02	203	84	16	13.8
		p	29	12	17	114	2.72	215	79	14	3.8

*Right ventricular systolic pressure.

pulmonary artery pressure by the cardiac output. After the resting measurements were obtained, the supine patients pedalled a stationary bicycle for 5 minutes at a constant rate and expired air and blood samples were collected during the last two minutes of exercise. The patients were then permitted a recovery period during which pulmonary artery or right ventricular pressures were visually monitored until they were once again at control levels. The patient was then given .8 mg. of atropine sulfate intravenously over a 2 minute period, and, 10 minutes later, the rest and exercise measurements were repeated. In 5 instances only rest or only exercise studies were performed.

Results

The results of the hemodynamic studies in these patients are shown in Table 1. Evidence of a pharmacological effect of atropine is provided by the fact that, after atropinization, most of the patients showed an increased heart rate both at rest and during exercise.

The patients were separated into three groups, depending upon the effect of atropine upon the total pulmonary resistance to blood flow. The majority of the patients had less than a 20 per cent change of pulmonary resistance and showed variable and small changes of pulmonary artery pressure after the administration of atropine. Three patients showed a fair response in that their total pulmonary resistance decreased from 20 to 46 per cent either during rest or exercise and, in each instance, there was some decrease of the pulmonary artery pressure. One had an unequivocally good response with a marked decrease of total pulmonary

TABLE 2 — RESULTS OF PULMONARY FUNCTION STUDIES

For each patient, the average value for MMF is listed, as well as the range of values measured over a period of 1-2 years.

Patient	Age	MMF l./sec. Mean	MMF l./sec. Range	Vital Cap. Per cent Normal	P_{ACO_2} mm.Hg. Rest	P_{ACO_2} mm.Hg. Ex.	D_{CO} cc/min/mm.Hg. Rest	D_{CO} cc/min/mm.Hg. Ex.	V_D/V_T Per cent Rest	V_D/V_T Per cent Ex.
Normal		4.0		100	40	40	15	>20	<30	<30
				No Response						
L. O.	61	.42	.38—.49	57	56	60	9.4	10.5	55	34
J. B.	64	.51	.38—.71	76	38	38	6.1	8.2	33	33
F. Me.	70	.23	.16—.28	44	40	54				
J. S.	55	.29	.24—.42	36	67		6.0		51	
F. M.	80	.52	.49—.58	54	42		7.0		26	
E. M.	64	.59	.43—.80	61	45	47	7.1	19.5	52	50
M. C.	58	.39	.31—.51	67	58		7.4		52	
L. M.	58	.33	.23—.33	42	51	54	4.9	5.7	46	45
				Fair Response						
G. W.	57	.62	.28—1.29	65	39	38	13.7	12.0	38	33
K. P.	54	1.01	.53—1.42	76	44	42	18.2	17.0	53	39
J. C.	65	.66	.49—1.12	53	37					
				Good Response						
T. M.	40	.51	.36—.93	41	48		9.0	7.8		

resistance consisting of both a decrease of pulmonary artery pressure and an increase of cardiac output after the administration of atropine.

Table 2 shows the results of the pulmonary function studies performed on these patients. In general, those who exhibited no response to atropine had clinical evidence of severe pulmonary emphysema. This diagnosis was supported by the physiological data which revealed sustained and severe airway obstruction, as evidenced by a low fixed MMF, a variable degree of abnormality of arterial blood gas composition and, with one exception, a very low diffusing capacity both during rest and exercise. The three patients who exhibited a fair response to atropine had a clinical diagnosis of bronchial asthma. Airway obstruction varied from mild to severe, and, in the two in whom it was measured, the diffusing capacity was less severely reduced than in the "No Response" group. The one who showed an unequivocally good response to atropine was the only patient in the group who had recently recovered from congestive heart failure. He had been admitted with venous congestion, edema and shortness of breath which had largely disappeared at the time of study. There was no evidence of left ventricular failure, and distinction between underlying asthma or emphysema was difficult. Although his MMF was not always as seriously reduced as in the "No Response" group of patients, there was sufficient evidence of chronic airway obstruction and diffusion limitation to suggest the diagnosis of pulmonary emphysema.

Discussion

The majority of the patients studied showed no significant beneficial effect on the pulmonary circulation from the administration of atropine. These were patients with a clinical and physiological diagnosis of chronic obstructive pulmonary emphysema. Since atropinization was without effect, vagotomy was not considered in these patients. Three with clinical and physiological evidence of bronchial asthma showed improved pulmonary hemodynamics after the administration of atropine. Although atropinization caused improvement in them, their disability was insufficient to warrant consideration of vagotomy. One who had recently recovered from congestive heart failure showed marked improvement after administration of atropine. He was the only candidate for vagotomy in the entire series.

It is quite likely, as implied by Abbott, that when a beneficial effect is observed it is in part mediated via reduction of airway obstruction with reduction in the intrathoracic pressure and coincident improvement of blood flow. In the one patient in whom there was a dramatic response to the administration of atropine, spirometric study before and after the administration of .8 mg. of atropine i.v. revealed an increase of MMF from .36 to .50 1./ sec. coincident with increase of the vital capacity from 1.43 to 2.30 1. Thus, improved hemodynamics might be expected to follow vagal block when bronchospasm is present, whereas patients with relatively fixed airway obstruction might not be expected to show improvement. The effect of atropine on pulmonary hemodynamics may provide a practical guide as to the advisability of vagotomy in the treatment of patients with chronic airway obstruction.

SUMMARY

The effect of atropine sulfate on pulmonary hemodynamics has been studied in 12 patients with chronic airway obstruction. In eight patients with clinical and physiological evidence of emphysema, there was no significant change of pulmonary artery pressure or cardiac index. In three patients with bronchial asthma, there was some decrease of pulmonary artery pressure and/or increase of cardiac index. In one with emphysema and recent congestive heart failure, there was a dramatic reduction of pulmonary artery pressure and increase of cardiac index.

RESUMEN

El efecto de la atropina en la hemodinámica pulmonar se estudió en 12 enfermos con obstrucción crónica de las vías aéreas. En ocho enfermos con evidencia clínica y fisiológica de enfisema no hubo cambio significante de la presión de la arteria pulmo-

nar o del índice cardíaco. En tres enfermos con asma bronquial hubo alguna disminución de la presión de la arteria pulmonar y/o aumento del índice cardíaco. En uno con enfisema y con reciente insuficiencia cardíaca congestiva, hubo una espectacular reducción de la presión de la arteria pulmonar y aumento del índice cardíaco.

RESUMÉ

L'effet du sulfate d'atropine sur l'hémodynamique pulmonaire a été étudié chez 12 malades atteints d'obstruction chronique des voies respiratoires. Chez 8 malades atteints d'emphysème clinique et physiologique prouvé, il n'y eut pas de modification significative de la pression de l'artère pulmonaire ou de l'index cardiaque. Chez 3 malades atteints d'asthme bronchique, il y eut une certaine diminution de la pression de l'artère pulmonaire et/ou une augmentation de l'index cardiaque. Chez un malade atteint d'emphysème et d'arrêt cardiaque récent, il y eut une réduction dramatique de la pression de l'artère pulmonaire et une augmentation de l'index cardiaque.

ZUSAMMENFASSUNG

Untersuchung der Wirkung von Atropin-Sulfat auf die haemodynamischen Verhältnisse der Lunge bei 12 Patienten mit chronischer Behinderung der Luftwege. Bei 8 Kranken mit physiologischen und klinischen Zeichen eines Emphysems trat keine wesentliche Veränderung des pulmonalen Cefässdruckes oder des cardialen Index ein. Bei 3 Kranken mit Bronchialasthma kam es zu einem leichten Rückgang des pulmonalen arteriellen Druckes und/oder Ansteigen des kardialen Index. In einem Fall mit Emphysem und kürzlichem Herzversagen mit Stauung kam es zu einer dramatischen Verringerung des pulmonalen arteriellen Druckes mit Anstieg des kardialen Index.

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A Study of the Maximal Ventilatory Flow Rates in Health and Disease

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A determination of the maximal volume of ventilation has become an integral measurement in the pulmonary function profile. This capacity becomes reduced with airway obstruction and when the stroke volume is reduced in the absence of airway obstruction. Such tests have also assumed added importance as a guide in the selection of candidates for operation and post-operative prognosis.

No test currently employed meets the ideal requirements. One of these requirements is that a high degree of patient cooperation should not be necessary for the success of the test. The procedure should be rapid and easily performed. The values should be reproducible. A practical consideration is that the instrument be relatively simple.

Since 1933, the maximal breathing capacity as described by Hermannsen[15] has been employed as the standard measure of ventilatory capacity. There are some variations in the techniques used for its performance, with a resultant large range of the reported mean values.[2,14] Cardinal is the need for full cooperation of the patient for a proper test.

With respect to these considerations, a single breath maximal effort procedure would appear to have distinct advantages. Although patient cooperation is again of prime importance, the brevity of the test makes sustained effort unnecessary, and fatigue is not a factor. The simplicity and rapidity allow the study of many patients in a minimum time. It is a reliable single breath method for ventilatory capacity, and allows the vital capacity to be simultaneously determined. A disadvantage, however, is its failing as an over-all performance test of ventilation, which the MBC does provide.

Our experience with the measurement of maximal expiratory and inspiratory flow rates since 1955 is the basis for the report which follows:

Materials and Methods

The subjects included in the study comprised normal subjects and patients with pulmonary disease. The normal subjects included a group of young individuals between ages 20 to 35 years, and a group of older individuals, 45 to 66 years of age. These subjects were house physicians, nurses, clinical workers, relatives, hospital employees and attending physicians. The patients were those ill with pulmonary sarcoidosis, and those having obstructive pulmonary emphysema. The patients with pulmonary emphysema were those who exemplified the classical problem of respiratory obstruction. Although primary chest wall and/or pleural derangements, and neurologic lesions have been studied these conditions are not included in the present study. The mean age of the patients having early sarcoid was comparable to that of the young normals; the

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patients having pulmonary emphysema were comparable in mean age to the sample of older normals. The sample size, sex distribution, mean ages and ranges are compiled in Table 1 along with all the other data pertinent to the study.

The apparatus used was a 9 liter valveless, low resistance spirometer, (Figure 1*) with a single 71.5 cm. length corrugated anaesthesia tubing for inspiration and expiration. This tube is fitted with a disposable cardboard mouthpiece with an internal diameter of 1.9 cm. An analysis of similar systems has demonstrated that the inertia develops a pressure 11 cm. water in the bell at the beginning of a forced expiration, but a negligible value occurs within 0.2-0.3 seconds. In the spirometer employed, a lower inertia pressure is developed because of the reduced weight of the bell. Bernstein has shown that recording artifacts in spirometer traces are related to the inertia of moving parts and the tendency of the water column to resonate.[2] He has shown that these may be minimized by reducing the mass of the bell, the length of the bell in relation to its cross sectional diameter, with thin cords and light pulleys of small radius, and by reducing the area of the air-water interface. The spirometer designated by him[2] and the one used in this laboratory are compared with the Knipping instrument (Table 2). The physical characteristics of the spirometer used by us resembles those of the spirometer designed by Bernstein. Minimal artifacts do occur in some of our records, but these are unimportant for they do not affect the measured part of the curve. The paper on which the record is inscribed moves rapidly at a speed of 26.1 mm. per second.

*Blodgett-Osborn spirometer, H. S. Osborn Company, Havertown, Pennsylvania, as described by Comroe, J.[7]

FIGURE 1: The 9 liter, low resistance spirometer is shown above. The paper speed is 26.1 millimeters per second. Note the relatively broad bell diameter and the small, light pulleys and suspension.

All determinations were done in a standing position. Control subjects and patients were instructed to take a maximal inspiration, insert the mouthpiece, purse the lips tightly around it, and exhale as rapidly and completely as possible into the spirometer. The examiner observes the trace and when the pen reaches the nadir of its travel indicating that the full vital capacity has been delivered, the patient is instructed to take a maximally rapid inspiration. The procedure is repeated until the form of the curve is constant. This rarely requires more than three or four attempts.

The maximal expiratory flow rate (MEFR) and maximal inspiratory flow rate (MIFR) are calculated from the slope of the trace. In practice we measure this slope not from its origin, but from a point on the curve arbitrarily chosen and representing an expired volume of 280 cc.* Reference to Table 1 again will show that during the 0-280 cc. expired volume interval there is submaximal flow which presumably includes the period when inertial forces of the chest, lung and spirometer system are being overcome. From the 280 cc. volume point a perpendicular line is dropped for a distance representing 500 or 1000 cc. of expired volume. A horizontal line then joins the curve from either of these points, forming a right triangle (Figure 2). The distance in mm. of this base (x) is measured. When the base is drawn at 1000 cc. volume as is most commonly done, the flow in liters per minute is designated as ME or MEFR 280 - 1280 or simply as ME or MEFR 1280 and is calculated from the simple formula: $\frac{26.1 \times 60}{X}$, where 26.1 mm. per second is the paper speed, 60 is seconds,

*This was chosen rather than the 200 cc. value recommended by Comroe because this volume appeared to be involved in the mechanical principles delaying the rate of volume flow for the spirometer system used.[7]

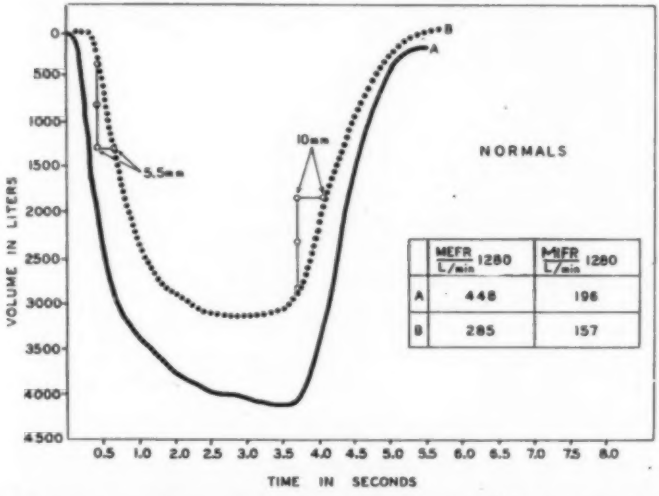

FIGURE 2: These representative curves in young people were chosen because they show flow close to the mean values for that group. A. 28 year old man, vital capacity 97.6 per cent of predicted. B. 97.3 per cent. The method of measurements is explained in the text under Material and Methods.

	NORMALS				SARCOID		EMPHYSEMA
AGE RANGE	20 - 35		45 - 66		19 - 50		37 - 79
AGE MEAN	29	26	55	52	32	31	61
SEX	Male	Female	Male	Female	Male	Female	Male
NUMBER	18	18	18	17	7	10	44
EFR_{0-200} cc. L/min.	211 ± 61	177 ± 54	153 ± 56	107 ± 32	188 ± 57	156 ± 42	89 ± 36
time, seconds	.088 ± .027	.102 ± .024	.124 ± .043	.171 ± .050	.099 ± .030	.119 ± .042	.226 ± .109
$MEFR_{200-760}$ cc. L/min.	470 ± 135	322 ± 98	304 ± 123	160 ± 51	310 ± 143	265 ± 104	66 ± 46
time, seconds	.069 ± .018	.103 ± .029	.120 ± .059	.216 ± .104	.121 ± .055	.134 ± .06-	.795 ± .658
$MEFR_{200-1200}$ cc. L/min.	477 ± 143	309 ± 88	305 ± 128	180 ± 59	290 ± 122	222 ± 88	53 ± 39
time, seconds	.136 ± .038	.211 ± .055	.242 ± .121	.391 ± .189	.249 ± .108	.331 ± .125	2.034 ± 1.503
$MEFR_{0-1}$ second	224 ± 37	172 ± 31	159 ± 32	118 ± 19	139 ± 37	125 ± 31	59 ± 24
$MIFR_{200-760}$ cc. L/min.	226 ± 66	165 ± 39	150 ± 43	135 ± 35	177 ± 74	156 ± 65	97 ± 38
time, seconds	.143 ± .042	.194 ± .046	.221 ± .080	.241 ± .077	.202 ± .085	.226 ± .085	.359 ± .138
$MIFR_{200-1200}$ cc. L/min.	248 ± 75	183 ± 42	178 ± 47	142 ± 43	204 ± 90	165 ± 63	98 ± 41
time, seconds	.263 ± .075	.345 ± .078	.369 ± .137	.442 ± .138	.350 ± .135	.417 ± .148	.712 ± .288
MBC L/min.	146 ± 21	103 ± 24	118 ± 33	75 ± 15	116 ± 37	83 ± 16	41 ± 19
Coef. Corr.:							
MBC-$MEFR_{200-1200}$ cc.	.69		.72		.76		.72

TABLE 1: The composition of the subject material and a summary of all observations made are shown above. For the explanation of abbreviations and qualifying subscripts see section of text under Material and Methods.

and X is the base of the triangle in millimeters. When the flow rate is calculated at 500 cc. along the perpendicular line, it is known as MEFR 280 - 780 or simply as $MEFR_{780}$. The formula is similar and again the flow is expressed in liters per minute. The latter calculation becomes useful in people with vital capacities below 1300 cc.* In practice, a transparent rule is used which quickly measures the base of the triangle and the corresponding flow is measured from a table. It is also possible to use a rule reading directly in terms of flow, if some reduction in the accuracy of measurement is accepted.† It will be seen that the rate as calculated represents a mean flow value over a specific volume interval on an arbitrarily chosen section of the curve. This is the steepest portion and as will be pointed out later, the values derived are actually very close to the true maximal flows.

For the purpose of study, we have also calculated the rate of flow after one second of expired volume. The one, two and three second timed vital capacities are easily derived from the measurement of expired volume at these specific times, and are expressed as a percentage of the patient's total vital capacity.

The maximal breathing capacity was performed on each subject after a suitable rest interval. In this laboratory we prefer to conduct this test with the patient breathing from a large, thin, air-filled rubber bag into the ambient air through a Hans-Rudolph valve. The resistance in the circuit is low. The change of volume at the end of a 15 second interval of breathing is measured for the determination. Corrections for body temperature and calculations for one minute are made for each determination.

Results

The maximal expiratory flow curve found in young normal subjects has been traced in Figure 2, A and B. Four sections can be distinguished. Initially, a brief portion, usually less than 280 cc. with a mean duration of less than 0.102 seconds ± 0.024 for young people, and 0.171 seconds ± 0.050 for the older age group. In patients with sarcoid, the mean duration of this interval is 0.119 second ± .042. Normal subjects of the same age have the same values. In emphysematous individuals the time for delivery of the first 280 cc. is prolonged, the mean value being .226 second ± .109.

The steepest most linear portion of the curve is inscribed during the next 0.5 - 1.0 liter of expired volume, and corresponds to the period of maximal expiratory flow during which the calculations are made. The difference between the $MEFR_{780}$ and the $MEFR_{1280}$ is not significant. The values and times are noted in Table 1. Flow rate at one second is much lower than that at the $MEFR_{780}$ or $MEFR_{1280}$. At one second the point of measurement is within the third or fourth portion of the curve. This is at the time of diminishing flow, but which is not so precipitous a fall of flow as in the fourth portion of the curve. In the last portion the nor-

*This was the point of measurement made in a study of young children. (Manuscript in preparation). The flow rate is expressed for liters/min. as recommended by Comroe and which is the more common expression found in the literature.

†Kory has recently described a transparent plastic rule which aids the measurement, decreases the ruled paper expense, and increases the accuracy of the measure: "A Rapid Method for Analysis of Spirographic Tracings," *Dis. of Chest* 33:5, 1958.

TABLE 2

	Old Spirometer Knipping	Bernstein Spirometer	Blodgett-Osborn
Bell			
material	brass	aluminum	aluminum
thickness, mm.	0.45	0.30	0.4
length, cm.	40	28.8	29.8
diameter, cm.	16.9	23.1	19.8
capacity, liters	6.0	9.0	9.0
weight, grams	868	250	586.5
Counterbalance			
weight, grams	828	200	308
Suspension			
material	metal chain	cord	wire
weight, grams	104	negligible	2.4
Total weight of moving parts, grams	1800	450	898
Pulley			
number used	one	two	two
material	duraluminum	perspex	wood
diameter, cm.	12.5	6.0	5.1
thickness, mm.	10	3.0	6.0
weight, grams	245	22.5 each	17.4, 17.8
moment of inertia, gm. cm.^{2}	4786	314	115
Width of inner water column, cm.	1.6	0 8	1.8
Inlet and outlet limb, internal, diameter, cm.	2.0	5.0	3.7
Flexible anesthesia tubing			
length, cm.			71.5
int. diameter, cm.			2.5
Disposable cardboard mouthpiece			
length, cm.			7.5
int. diameter			1.9
Drum speed, mm./sec.	12.4	28.5	26.1

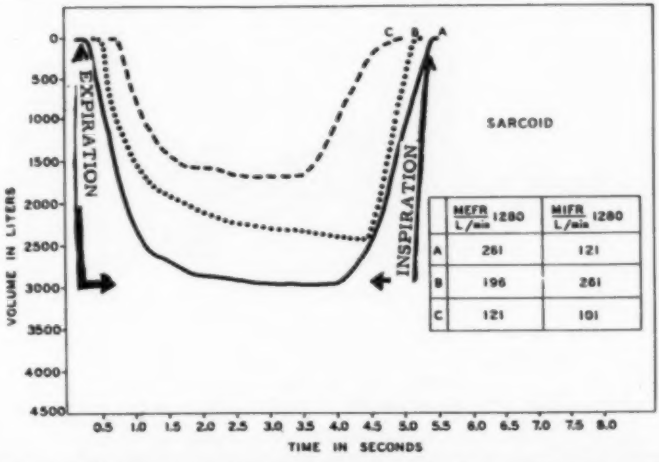

FIGURE 3: Three traces in patients with sarcoid. A. 31 year old woman with a vital capacity of 94.4 per cent. B. A 22 year old man with a vital capacity of 76.1 per cent. C. 26 year old woman with a vital capacity of 53.0 per cent.

mal expiratory check valve mechanism operates. Usually, the entire vital capacity can be delivered within less than four seconds.

The MEFR curve in sarcoid has the same form as in normal individuals. Patients having sarcoid share with normal people the ability to increase sharply the rate of flow following the initial 280 cc. volume interval. Although the mean age of the patients with sarcoid is comparable with that of young normal subjects, the mean flow rate values are lower and fall in the range of the older normals. The $MEFR_{780}$ is 310 liters per minute ± 143 for the men and 265 liters per minute ± 104 for the women. The time of delivery of the required volumes is not greatly prolonged. In Figure 3, three typical curves are shown. It may be seen that in restrictive disease the MEFR is influenced by the vital capacity. Patients with a normal or near normal vital capacity have higher flow rates, but those with marked reduction in capacity have also reduced measured flows. In general, sarcoid patients have $MEFR_{780}$ and $MEFR_{1280}$ of the same order. Where the vital capacity is greatly reduced the 1280 cc. point of measurement may fall on the portion of the curve where the slope has flattened. Thus the $MEFR_{1280}$ will be appreciably less than $MEFR_{780}$. This finding is best seen in the group of women. A graphic summary of the sarcoid data with the normal young controls of comparable age is presented in Figure 4.

In emphysema striking alterations in the form of expiratory flow curve occur. Representative traces are shown in Figure 5. As previously mentioned the mean rate of flow during the first 280 cc. expired volume was significantly lower than in the other groups. Patients with emphy-

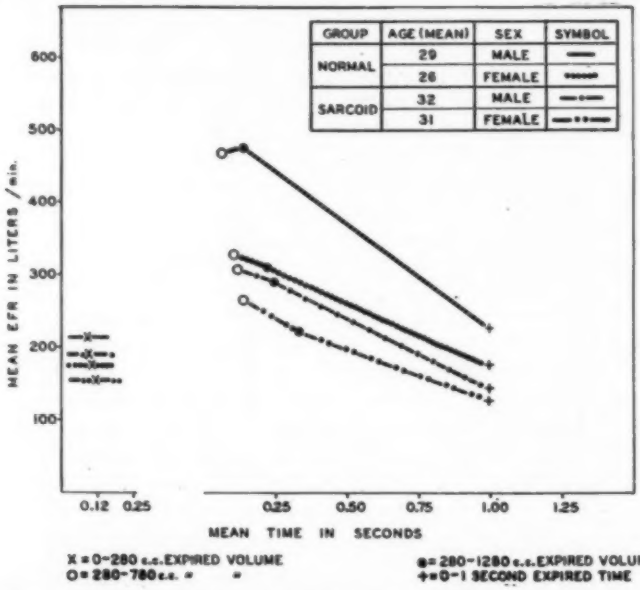

FIGURE 4: Mean flow values and delivery times for all portions of the curve measured are shown for the patients with sarcoidosis according to sex with the young normals who are of comparable age as reference. Note that the ability to sharply increase the flow rate after the initial period is comparable to that of the normals.

sema are unable to increase their flow rate over the next liter of expired volume. Flow decreased during this interval from a rate of 89 liters per minute ± 36 during the first 280 cc. of expired volume fell to 66 liters per minute ± 46 at $MEFR_{780}$ and still further to 53 liters per minute ± 39, at $MEFR_{1280}$. These marked reductions in flow were associated with an increase in the time of delivery of the 780 cc. and 1280 cc. volumes. This contrasts greatly with normal male subjects. In Figure 6 the data is presented graphically. The mean time to $MEFR_{1280}$ is 2.034 seconds ± 1.50.

In traces A and B of Figure 5 arrows indicate points on the curves where an initial rate of relatively rapid flow is abruptly terminated. The subsequent portion indicates that the patient is exerting a prolonged effort during which he is able to deliver only small increments of volume. Under these circumstances the time to deliver the full vital capacity is much increased. Individuals with the smaller vital capacities have even lower flow rates. The lowest flow is achieved in this type of emphysematous patient, because not only is the vital capacity small but there is also obstruction. For example in sarcoid a vital capacity of 76 per cent has an MEFR of 261 liters per minute (B, Figure 3), whereas an emphysematous patient with the same vital capacity has an MEFR of only 76 liters per minute (A, Figure 5).

In general the MIFR curve tended to approximate a straight line and a maximal inspiration required less time than a maximal expiration, although in both age groups of normal subjects the men had mean MIFR's about 55 per cent as great as their MEFR's. Young women tend to behave in the same way, but the difference is less in older women who exhibited the smallest expiratory flow rates of all subjects. The $MIFR_{1280}$ is greater than the $MIFR_{780}$ suggesting that peak inspiratory flows occur later than peak expiratory flows. The terminal deceleration corresponding to the fourth part of the expiratory curve is absent normally on the inspiratory curve.

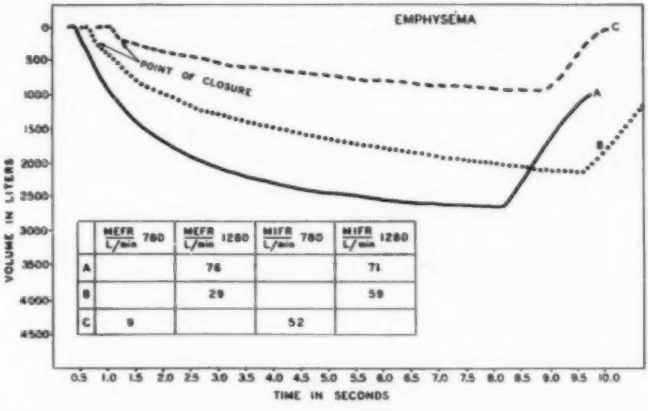

FIGURE 5: Three illustrative curves in emphysema patients. A. 66 year old man with vital capacity of 77 per cent. Note difference in rate and in form of the trace when compared with the sarcoid patient with an identical per cent of predicated vital capacity. B. 63 year old man with vital capacity of 63 per cent. C. 56 year old woman with vital capacity of 37 per cent.

Moderate reduction of the MIFR is present in male sarcoid patients, but the form of the curve is normal.

A maximal breathing capacity was determined on all normal subjects and patients. The mean values are shown in Figure 1. The correlation between this test and the MEFR varied from .69 to .72 in the normal groups and in emphysema, and it was .76 in the sarcoid patients. This correlation is discussed below.

Discussion

The MEFR affords a fast, practical and reliable estimate of ventilatory function. It requires minimal demands on the chronically ill patient, and reduces appreciably the degree of cooperation required in testing an essentially voluntary function.

The values for maximal flow rate show a large standard deviation from the mean. As cited, the coefficient of variability for this test is greater than for the maximal breathing capacity among these same patients and in other studies.[16] However, the data are uncorrected for age, vital capacity, height and body surface area. In a study in this laboratory of the maximal expiratory flow rates in 1159 school children from 6-14 years, the correlations between MEFR and age were 0.732 for boys and 0.735 for girls.[27] For vital capacity the correlations were 0.790 and 0.778 respectively. The regression equations for the MEFR in these children have a standard error of $\pm$ 43 or about 18 per cent.

Greater accuracy in the estimation of the observed MEFR in normal subjects can be attained by increased speed of the kymograph drum. With low rates of flow, the error of measurement is small, so that at a rate of 156 liters per minute a 0.5 millimeter inaccuracy results in a deviation of only 8 liters per minute. At lower rates of flow a difference of as much as 3-4 millimeters is of little consequence.

Two other observations are considered important in evaluating traces with low flow rates especially with respect to the distinction between restrictive and obstructive disease. In restrictive disease the rate of flow tends to diminish with the vital capacity but the form of the curve is basically unaltered. This tendency is noted in Figure 3. Furthermore, in almost all patients with sarcoidosis the rate of flow increases after the inertial period of the spirometer is overcome. This is illustrated in Figure 4 where the mean flow rates in this group at 0-280 cc. expired volume are compared with $MEFR_{780}$ and $MEFR_{1280}$. Patients having emphysema fail to show this characteristic when their mean values are plotted. (Figure 6).

The marked deformity of the curve results from the check valve mechanism ('point of closure') described by Dayman.[8,9] Dayman states that the tension of the normal lung and airways both reach a maximum of 20-30 grams per square centimeter at maximal inspiration. The caliber of the air passages varies with lung tension and inflation. A point of closure is produced on the record by the forced expiratory effort.

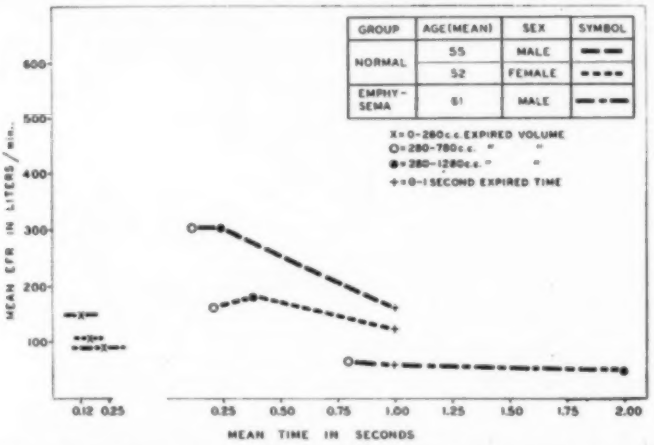

FIGURE 6: Mean flow values and delivery times for all portions of the curve measured in men emphysema patients who are compared with normal men and women of comaparable age. Note the low flow rates and the deformity of the curves, the 'point of closure' (see text, Discussion) and the decline in flow rate after the initial interval contrasting with the behavior of the normal and sarcoid groups.

Similarly in the fourth portion of the expiratory flow curve, when most of the vital capacity has been expelled and the patient is exerting a violent pressure to "squeeze out" the rest, it is likely that the low rate of flow is due to the operation of a check valve mechanism.

Dayman points out further that in emphysema, lung tension rises only to 10 grams per square centimeter or even less on full inspiration, so bronchial distension is lacking. Thus bronchioles collapse under slight transthoracic pressure. This results in a diminution of pressure within the downstream airways as far cephalad as the intrathoracic portion of the trachea, and promotes partial collapse at these levels. A forced expiration as in the MEFR procedure, with rapid application of high intrathoracic pressures, brings this mechanism into play. After the point of closure, continued expiratory effort results in extremely small increments of volume.

Considerable disagreement regarding the form of the fast vital capacity curve in normal individuals has arisen. Tiffeneau and Drutel[26] described an initial rectilinear segment over approximately the first 2000 cc. of expired volume expelled at a rate of 300 liters per minute, which was followed by a curvilinear portion. Hirdes and van Veen[16] concluded that the first part of the record is a straight line and Kennedy[17] described a relatively steep and linear first fraction breaking away at the 'critical point' into a less steep second fraction. Bernstein[3] and D'Silva[10] have written that these complicated curves are recording artifacts which are eliminated by a spirometer of improved design[1,3] whose specifications are listed in Table 2 of this paper. In their view the curves are always smooth and concave upward, differing only in the time required to expel the fast vital capacity. The similarity to an exponential curve is stressed.[10] However, it is apparent even in their work that this is not always so.[3] Shephard,[22,23] using both spirometric and pneumotachographic methods has concluded that the records are not always smooth curves and that in addition to spirometer artifacts, the technique of the subject and varying patterns of gas flow are of considerable importance. The spirometer used in this laboratory eliminates most of the objectionable features outlined by Bernstein.[3] Although some of the MEFR curves were smooth, it was more common to find a rectilinear segment following the inertial shoulder. The almost identical values for $MEFR_{780}$ and $MEFR_{1280}$ in many normal men would appear to support these observations since if the flow rate were the same for two successive expired volumes of the same expiration, the result would have to be a straight line.

The forced expiration curve has been analyzed in many ways. Tiffeneau et al[25] measured the one second volume which he termed the "capacite utilite" per second and when divided by the total vital capacity this is expressed as the percentage of the vital capacity that is easily utilizable. He also attempted to predict the maximal breathing capacity from the one second volume by multiplying it by a factor of 30 on the assumption that the MBC would be performed at a respiratory frequency of 30 per minute.[24] His values were low by about 20 per cent. Gaensler estimated that the proportion of the vital capacity expelled in one second is 82.7 per cent[12] a figure practically duplicated by D'Silva.[10] Gaensler found the correlation between the maximal breathing capacity and timed vital capacity to be 0.88 at one second, 0.79 at two seconds, 0.25 at three seconds, and 0.56 for the total vital capacity.

Subsequent authors directed their efforts towards the prediction of the maximal breathing capacity from fast vital capacity curves, and measurements were made at 0.5 seconds,[19,21] 0.75 and 1.5 seconds,[17] 0.43 and 0.6 seconds and 1.0 seconds,[16] and 2.0 seconds.[20] It is apparent that the MBC is performed over specific sections of the forced expiratory and inspiratory slopes. A high correlation between the MBC at any determined rate of breathing and the forced expirogram is found if one measures off a segment of the expirogram corresponding to the time available for expiration at that specific respiratory frequency. Thus Kennedy[17] found a correlation of 0.927 between the MBC at 40 per minute and the expiratory flow rate over 0.75 seconds, whereas D'Silva[10] also showed a high correlation between the MBC at 30, 50, or 70 breaths per minute and the 1.0 second, 0.6 second and 0.43 second segments of the expiratory trace respectively. Bernstein[4] in a thoughtful discussion of the subject offered theoretical and experimental reasons why the slope of the inspiratory trace, the inspiratory-expiratory time relationships and the level of inspiration at different frequencies should all be taken into consideration, and he reports a correlation of 0.972 between predicted and observed values for MBC at rates from 20-100 per minute. Shephard has made similar recommendations.[22] Our own correlations (Figure 2) between MBC and $MEFR_{1280}$ are random. No attempt was made to record the rate or depth at which the MBC was performed or to measure the MEFR with the view to improving the correlation as outlined above.

Our own objectives in measuring the flow rate have differed from the purposes of the studies mentioned in the previous paragraph. Interest in predicting the MBC, has not been held but rather focus has been placed in determining the maximal expiratory flow as an independent pulmonary function test. Leuallen and Fowler[18] had similar objectives. Using a pneumotachograph they concluded that peak flow rates of 8-11 liters per second for men and 5-7 liters per second for women occur within 0.1 second. During a comparable interval there was a peak flow rate of 1-3 liters per second in patients with emphysema. They concluded that the spirogram is an unsuitable instrument for recording initial flow because of its inertia, and instead measured the middle half of the expiratory flow curve for which they found values of 4.5 liters per second in men and 3.7 liters per second for women. From the traces they have reproduced

it is apparent that the end of their "middle-half" segment is at the one second mark. Our own data as well as observations of others[12,13] indicate that the flow at one second falls to about 40 to 60 per cent of the maximal value and by computation their mid-expiratory flow rate for young men is 55.3 per cent of our peak values. We question whether the time of onset of the peak velocity makes the spirometer an unsuitable instrument for measuring this parameter. Shephard,[13] in a pneumotachographic study found that the peak expiratory flow occurred at 0.51 seconds and inspiration at 0.58 second. When this was repeated with a spirometer in the circuit an actually earlier peak flow was recorded on the spirometer, 0.21 second for expiration and 0.38 second for inspiration. The expiratory lag of his Knipping spirometer was estimated at 89 ± 9 milliseconds. The improved design of our instrument makes it seem likely that its lag is even less and inspection of the form of the 0-280 cc. portion of the curve would appear to confirm this. The inertial period in young men is invariably less than the mean of .088 second ± .027 necessary to deliver the 0-280 cc. volume. It will be recalled that the $MEFR_{780}$ or the $MEFR_{1280}$ and usually both are on the fast rectilinear portion of the slope, and peak flow not infrequently has occurred at $MEFR_{780}$. Although we feel that this point is reached earlier than Shephard's observations indicate it must not commonly take less than 0.15 seconds even in the young men with the fastest flow rates and the shortest delivery times. With respect to the mean values for maximal expiratory flow, our figure of 477 liters per minute in young men compares favorably with the 400 liters per minute for one liter point quoted by Comroe[7] and even more favorably with the 450 liters per minute in young RAF personnel.[13] With the pneumotachograph, Shephard's same subjects not only had the later onset of peak flow as noted above but their maximal values were only 291 liters per minute in expiration. This may be due to the role of increased resistance of the spirometer circuit in enhancing the linear velocity.

We have found little practical application for the inspiratory flow rate, and have had no opportunity to study it in cases of laryngeal or tracheal obstruction. The inspiratory trace tends to retain a more linear form and the total delivery time is shorter than in the expiratory trace. Tiffeneau[25] measured the inspiratory flow at 500 liters per minute and Comroe[7] published the same figures of 400 liters per minute for both inspiratory and expiratory flow. Our findings agree with Shephard,[13] that the time of peak flow in inspiration is longer than the peak flow in expiration but that maximal flow is less. Like Shephard's subjects the young men in this study had MIFR values of about 55 per cent of the MEFR.

Diminished lung compliance is a probable factor affecting the reduced MIFR in male patients with sarcoidosis, but its main effect is on the MEFR values. In emphysema the MIFR is reduced to the greatest degree. The loss in vital capacity, reduction in compliance and the relatively raised end expiratory level at which inspiration is started all contribute to the low inspiratory flow rates.

SUMMARY

1. The maximal expiratory and inspiratory flow rates, abbreviated as the MEFR and MIFR is a rapid, practical test and compared to the maximal breathing capacity less demanding on patients who more willingly offer full participation and the required maximal effort. It is only rarely that the test cannot be done because of the patient's clinical condition.

2. The initial 1000-1500 cc. of expired volume is often represented as a steep rectilinear line of maximal flow, and the $MEFR_{780}$ and $MEFR_{1280}$ are derived from this segment.

3. The MEFR decreases with age, and within the same age group women have lower flow values than men. The same is true of the MIFR which in young normals and elderly men is approximately 55 per cent of the MEFR, but older women have a proportionately higher MIFR/MEFR ratio due to a greater fall in MEFR.

4. The correlation of maximal expiratory flow rate and maximal breathing capacity in all groups is reported, but for reasons outlined in the paper it is not as good as in other studies whose primary purpose was to correlate the two tests. The MEFR should be performed as an independent pulmonary function test and not as an indirect estimate of MBC.

5. The normal range of the $MEFR_{280-1280}$ was 477 liter per minute ± 143 liters per minute for men between 20-35 years, and 304 liters per minute ± 123 liters per minute for men older than 45. For women 309 liters per minute ± 88 liters per minute and 180 liters per minute ± 59 liters per minute for the respective age distribution. For abnormals it has shown considerable reduction, but marked restrictive disease measurement at $MEFR_{280-780}$ will give normal values. The explanations for this are described.

RESUMEN

1. Los volúmenes máximos expiratorios e inspiratorios, abreviados así: MEFR y MIFR, constituyen una prueba práctica comparada con la capacidad respiratoria máxima, menos exigente para el enfermo que de mejor gana ofrecen su cooperación y el esfuerzo máximo requerido. Sólo rara vz la prueba no puede hacerse a causa del estado clínico del enfermo.

2. El volumen inicial de 1000-1500 c. c. de aire expirado se representa a menudo como una línea recta ascendente de flujo máximo y el MEFR (780) y MIFR (1280) se derivan de este segmento.

3. El MEFR decrece con la edad y dentro del mismo grupo de edad, las mujeres tienen más bajos valores que los hombres. Lo mismo ocurre con el MIFR en los jóvenes normales y en los viejos es aproximadamente de 55 por ciento del MEFR, pero en las mujeres ancianas tiene una relación MIFR/MEFR proporcionalmente más alta debido a una caída mayor de MEFR.

4. La correlación de MEFR y la capacidad respiratoria máxima en todos los grupos, se refiere, pero por las causas señaladas en el trabajo, no es tan buena como en otros estudios cuyo objeto principal fué correlacionar las dos pruebas.

El MEFR debe llevarse a cabo como una prueba funcional pulmonar independiente y no como una manera de estimar la MCR (Capacidad máxima respiratoria).

5. La variación normal de MEFR (280-1280) fué de 477 litros por minuto más o menos 143 por minuto para hombres entre 20 y 35 años y 304 litros por minuto más-menos: 123 litros por minuto por hombres mayores de 45.

Para las mujeres, 309 litros por minuto más-menos 88 litros por minuto y 180 litros por minuto más-menos 59 litros por minuto en las respectivas edades. Para las personas anormales se ha mostrado una reducción considerable pero una medida restrictiva acentuada en la enfermedad como MEFR (280-780) dará valores normales. Se dan las explicaciones para esto.

RESUMÉ

1. Le taux de capacité maximale expiratoire et inspiratoire est un test rapide et pratique, si on le compare à la capacité respiratoire maximale. Elle exige moins du malade qui offre plus volontiers une coopération totale et l'effort maximal demandé. Ce n'est que dans de rares cas que le test ne peut pas être pratiqué à cause de l'état clinique du malade.

2. Les premiers 1,000 ou 1,500 cc du volume expiré sont souvent reprèsentés comme une ascension en ligne droite du débit maximal et les indices 280 et 1280 sont dérivés de ce segment.

3. Le taux de capacité maximale expiratoire décroit avec l'âge et chez des malades du même âge, les femmes ont des valeurs plus basses que les hommes. Il en est de même pour la capacité maximale inspiratoire qui, chez les jeunes normaux et les hommes plus âgés est approximativement de 55% du taux de capacité maximale expiratoire, mais les femmes âgées ont un quotient capacité maximale inspiratoire/capacité maximale expiratoire plus élevé du à la chute plus grande de la capacité inspiratoire.

4. Le rapport entre taux de capacité maximale expiratoire et capacité respiratoire maximale est rapporté pour tous les groupes mais pour des raisons esquissées dans l'article, il n'est pas aussi bon que dans les autres études, dont le premier dessein était de mettre les deux tests en corrélation. Le taux de capacité maximale expiratoire devrait être pratiqué comme un test de la fonction pulmonaire indépendant, et non comme une estimation indirecte de la capacité respiratoire maximale.

5. L'étendue normale de la capacité maximale expiratoire 280-1280 est de 477 litres par minute ± 143 litres par minute pour les hommes âgés de 20 à 35 ans, et 304 litres par minute ± 123 litres par minute pour les hommes de plus de 45 ans. Pour les femmes, 309 litres par minute ± 88 litres par minute et 180 litres par minute ± 59 litres par minute selon les âges respectifs. Pour les individus anormaux, on a constaté une réduction considérable, mais en cas d'affection grave restrictive, la mesure de la capacité maximale expiratoire donnera des valeurs normales. Les auteurs fournissent les explications de ce pnénomene.

ZUSAMMENFASSUNG

1. Die Gewinnung der Werte für die maximale Ausatmungs — und Einatmungs-Luft (MEFR und MIFR) stellten einen schnellen und praktischen Test dar und entsprechen dem Atemgrenzwert, ohne jedoch die gleichen Anforderungen an den Patienten zu stellen, der sich so eher zur vollen Mitarbeit und der notwendigen maximalen Bemühung bereit findet. Nur selten kommt es vor, daß die Probe nicht vorgenommen werden kann, weil es der Zustand des Kranken nicht erlaubt.

2. Die ersten 1000 bis 1500 ccm der Ausatmungsluft stellen sich oft dar als eine gradlinige und steil ansteigende Kurve des Maximalwartes, und die Werte für $MEFR_{780}$ $MEFR_{1280}$ werden von diesem Segment abgeleitet.

3. Die MEFR nimmt mit dem Alter ab, und innerhalb der gleichen Altersgruppe liegen die Werte bei Frauen niedriger als bei Männern. Das Gleiche trift zu bei der MIFR; sie beträgt bei jüngeren, gesunden und älteren Männern ungefähr 55% der MEFR. Jedoch liegt das Verhältnis von MIFR/MEFR entsprechend höher bei älteren Frauen infolge eines größeren Abfalles des MEFR-Wertes.

4. Wiedergabe der Korrelation der maximalen Ausatmungsluft zum Atemgrenzwert in allen Gruppen; aber, aus in der Mitteilung selbst näher angeführten Gründen, ist sie nicht so gut wie in anderen Untersuchungen, deren Hauptzweck in der Korrelation beider Teste bestand. Die Bestimmung der MEFR sollte als ein sibständiger Lungenfunktionstest vorgenommen werden und nicht als ein Verfahren zur indirekten Bestimmung des Atemgrenzwertes.

5. Der normale Spielraum des $MEFR_{280-1280}$ betrug 477 Liter pro Minute ± 143 Liter pro Minute für Männer zwischen 20 und 35 Jahren, und 304 Liter pro Minute ± 123

Liter pro Minute für Männer im Alter über 45 Jahren. Für Frauen 309 Liter pro Minute ± 88 Liter pro Minute und 180 Liter pro Minute ± 59 Liter pro Minute für die entsprechende Altersverteilung. In von der Norm abweichenden Fällen ergibt sich eine beträchtliche Herabsetzung, jedoch ergeben durch Krankheit ausgesprochen eingeschränkte Messungen des MEFR 280 - 780 doch normale Werte. Die Erklärungen für diesen Umstand werden gegeben.

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Reduction of Irregular Discharge Rates in a Tuberculosis Hospital

Impact of a Coordinated County Health Department and Tuberculosis Hospital Program Upon Unapproved Discharges.

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Irregular discharges have long plagued tuberculosis hospitals and entire communities. Inquiries into the problem have demonstrated numerous causes. These fall into two major categories: (1) intrinsic: that is, those problems within the patient that push him out of the hospital; and (2) extrinsic: those that operate outside the patient, either within or beyond the hospital setting, to pull the patient out of the hospital. These forces are of different strengths and set up conflicts of varying intensity.[1]

In most discussions of irregular discharges, attention centers upon internal tensions of the patient, and the rapport between him and the hospital staff. Usually ignored until too late is the responsibility of the patient to his community, and the reciprocal interest of the community, through its organized health services, in the health of the individual as a factor in the health of the community.[2]

The present observations incorporate data derived from the tuberculosis department of a general hospital in Polk County, Iowa spanning 12 years from January 1, 1946 through December 31, 1957. The personnel and operation of the unit have been remarkably constant throughout the period. During 1951, tentative approaches were made to initiate a home-care program,† extending hospital services into the home. August of that same year marked an innovation for the community: appointment of a full-time director of public health who established a comprehensive city-county health organization. This step permitted wider application of the home treatment concept. The new program incorporating early release from the hospital became fully operative by January 1952. The following month investigators reported a new oral medication, isoniazid, which dramatically improved the outlook for the chemotherapy of tuberculosis and gave additional support to the plan.

The early discharge of patients from the hospital with continuation of treatment at home demands fulfillment of two major conditions: (1) health department approval after the infectiousness of the tuber-

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†The home-care plan developed along identical lines set forth by the Committee on Therapy, Americal Trudeau Society.[3] This statement stresses preliminary hospitalization for control of the disease process and for teaching the patient its meaning; adequacy of the home; active interest of the family; assurance of consistent prolonged medical supervision; and return to hospital for control observations.

The important difference, however, is that the home-care program in this community stems from the concept that tuberculosis treatment is a phase of the community wide tuberculosis control, which, in turn is a basic responsibility of community public health group. The official health agency, therefore, has a prominent part in a coordinated home-care program.

culous process is under control; and (2) existence of suitable home conditions that are adequate to the necessities of medical management.

In order to maintain close supervision, the patients periodically returned to the hospital for collection of necessary laboratory specimens. Although this increased the total number of admissions to the hospital, these patients have been separated as "laboratory admission."

All patients who left the hospital during the 12 years January 1946 through December 1957 were reviewed. (Table 1). December 31, 1951 divided the study into two successive comparable six-year periods, the earlier one without benefit of coordination with the local health department; the later one reflecting its effects.

The number of irregular discharges is compared with the effective patient population* for each period. Observations on the length of stay of these patients and estimate of communicability through bacteriological study fill out the picture. Some indications of what finally happened to these patients complete the report.

As Table 1 demonstrates, a distinctly favorable shift occurred in the number of patients who were discharged with approval, from 204 (56.4 per cent) of 362 in the first group to 282 (78.6 per cent) of the 359 in the second sexennium. At the same time, 88 (24.3 per cent) of the first group left against advice, in contrast to 34 (9.5 per cent) of the second group.

These patients in the irregular discharge classification remained in the hospital for varying periods, as is shown in Table 2.

It is readily apparent that almost half left within the first 90 days of hospitalization, viz., 38 (43.2 per cent) of 88; and 16 (47 per cent)

TABLE 1 — DISCHARGE CLASSIFICATION OF 1,097 PATIENTS RELEASED BETWEEN JANUARY 1946 AND DECEMBER 1957, GROUPED IN TWO SUCCESSIVE SIX-YEAR PERIODS.

	Group 1 (No Home Care Program)		Group 2 (Home Care Program)		Total
	Number	Per cent of Effective population	Number	Per cent of Effective population	
Approved Discharge	204	56.4	282	78.6	486
Disapproved Discharge	88	24.3	34	9.5	122
Died	70	19.3	43	11.9	113
Effective patient population*	362		359		721
Transferred to other hospitals	58		59		117
Laboratory Admissions	0		178		178
Non Tuberculous	23		58		81
Total	443		654		1,097

*The effective patient population designates those who were eligible to remain for treatment of tuberculosis. It removes from consideration the substantial group admitted for diagnostic studies only and found not to have active pulmonary tuberculosis; as well as a group who, because of county residency requirements, were transferred to other hospitals for care.

TABLE 2 — DURATION OF HOSPITALIZATION OF 122 PATIENTS WHO LEFT AGAINST MEDICAL ADVICE, DIVIDED INTO TWO SUCCESSIVE SIX-YEAR PERIODS.

Length of Hospital stay in days	Group 1 1946 — 1951 No.	Per cent	Group 2 1952 — 1957 No.	Per cent	Total Groups 1 and 2 No.	Per cent
1 day or less	5	5.7	1	2.9	6	4.9
2 — 30	16	18.2	8	23.5	24	19.7
		(23.9)		(26.4)		(24.6)
31 — 90	17	19.3	7	20.6	24	19.7
	38	43.2	16	47.0	54	44.3
91 — 180	15	17.0	5	14.7	20	16.4
181 — 270	7	8.0	4	11.8	11	9.0
271 — 365	10	11.4	5	14.7	15	12.3
	32	36.4	14	41.2	46	37.7
More than 365	18	20.5	4	11.8	22	18.0
Totals	88		34		122	

of 34. Indeed, with further analysis, the first month becomes a highly critical period when approximately one-fourth of the group left; 21 (23.9 per cent) of 88; and 9 (26.4 per cent) of 34.

Even with the persuasive factors of home-care and health department support, the proportion of those leaving the hospital in the first 30 to 90 days continued unchanged in the two periods, although the actual numbers decreased impressively.

Home-care usually cannot go into effect until at least two months of hospitalization have passed, and in most instances the requirement is from three to six months according to previous studies.[4] Nevertheless, introduction of a policy of early discharge from the hospital to home-care, thus deliberately shortening the hospital stay, has resulted in weakening both the intrinsic and extrinsic factors that impel patients to leave the hospital without medical or health department approval.

TABLE 3 — FOLLOW-UP OF 122 PATIENTS WHO LEFT THE HOSPITAL AGAINST MEDICAL ADVICE DURING TWO SUCCESSIVE SIX YEAR PERIODS, JANUARY 1946 THROUGH DECEMBER 1957.

	Group 1 1946 — 1951 No.	Per cent	Sput.+	Group 2 1952 — 1957 No.	Per cent	Sput.+	Totals
Returned to hospital	19	21.6	13	14	41.1	4	33
To Private Physician	17	19.3	7	9	26.4	3	26
To Other Hospitals	10	11.4	5	1	2.9	1	11
Left the State	4	4.5	1	0	0	0	4
Died	10	11.4	7	1	2.9	0	11
No follow-up, or not found	28	31.8	9	9	26.5	2	37
Totals	88		42	34		10	122
			(47.8%)			(29.4%)	

Very likely, discouragement, failing health, the wish to try a different climate, or other medical supervision account for the rise in the figures of those who left after more than a year in the hospital. Public health implications of this study are important since in the first six years, 42 (47.7 per cent) of 88 leaving without approval had positive sputum; while in the second period, fewer than one-third 10 (29.4 per cent) of 34 were positive. Numerically, too, this reduction represents 10 patients to be pursued actively because of positive sputum, only one-fourth as many as in the first six-year period. This is set forth in Table 3.

For example, Mrs. A. G., a woman with known active pulmonary tuberculosis, left the hospital on two occasions, in 1947, after staying less than a day. She asserted that she just couldn't bring herself to remain. There was no health department authority to insist on hospitalization.

In 1954, when she returned to the hospital at the request of a representative from the health department, she remained without protest or attempt to leave until discharge was approved 16 months later. When asked why she accepted hospitalization so readily, she replied, simply, "They said I had to stay."

Another, F. S., hospitalized for more than two years, left against medical advice in 1956, and then returned, only to leave after another 26 days within the hospital. His next admission was under court order obtained by a representative of the health department. The patient made no further attempt to leave, but was transferred at his request to another hospital. Nearly a year later, he violated the court order, left the hospital, and has effectively disappeared.

Such patients typify a number of key problems in tuberculosis work. Foremost among these is patient acceptance of the diagnosis of tuberculosis and its implications for himself and for his family. Once this is achieved, the place where treatment is carried out becomes a subordinate matter.

An integral part of health department function is to augment the doctors' emphasis upon the patient's responsibility to his family and to the community, as well as to himself.

Of equal importance is the fact that tuberculosis as a communicable disease is a concern of the community. It requires legal re-inforcement of health department authority to cause patients to be detained in isolation.

Operating against these medical factors are those many overwhelming emotional and sociological circumstances, such as removal of the patient from home; changed work and income status of the patient; new financial stresses; separations that are long in both time and distance; types of disease that fortell prolonged and even indefinite hospitalization.

The final part of the inquiry has to do with what happened to the patients who left against advice. Some went immediately to other states and were lost to follow-up; others left the county but remained under medical supervision or were seen from time to time by members of the State Health Department organization. Some had deteriorated steadily and their deaths were later reported. Some returned to the hospital for treatment, either voluntarily, or pushed by members of the family, or ordered by the local health department.

In the earlier group 19 of 88 returned to the hospital while 14 of 34 in the later group came back. Thirteen of those 19 had positive sputum, while four of the 14 were positive. A small, but substantial group was reported under private medical care.

No follow-up was obtained in 37 instances, 28 of which occurred in the earlier group. Nine in Group 2 could not be located by the health department.

Twelve persons whose names appear more than once are called "repeaters" since each entry was followed by a disapproved discharge. In the earlier group this amounted to nine persons as contrasted with three in the second six year span. (Obviously, the repeaters of the second span returned in that same period. Of those in the first period, three returned during the first year, three in the next five years, and three in the following span).

Most of these had been in the hospital for prolonged periods. Six of the 12 are now dead. To some extent, this suggests that these patients sensed a hopelessness for recovery and left the hospital because it became intolerable to them. On the other hand, these were the patients who, by their very actions, had not made getting well their major striving.

The strength of health department authority is noteworthy among the repeaters and may be the most important factor in reducing their number during the second six year period.

This coordination of effort of local public health services and medical care, both in the hospital and in the patients' homes is founded on a sense of mutual responsibility in the control of an important communicable disease, tuberculosis.

SUMMARY

1. Of 1,097 patients discharged from the tuberculosis department of a public county hospital within a 12-year period, 122 left against medical advice.
2. Disapproved discharges decreased from 88 (24.3 per cent) in the first six years to 34 (9.5 per cent) in the second six years.
3. Open, infectious patients numbered 42 (47.8 per cent) of 88 in the first group and 10 (29.4 per cent) of 34 in the second group.
4. Reasons for this favorable change are:
   a. development of an active city-county health department under a full-time director,
   b. initiation of a home-care plan and abbreviated hospitalization,
   c. constant awareness of tuberculosis as fundamentally a communicable disease, requiring: intimate coordination of hospital, home, medical, nursing, and public health services.

RESUMEN

1. De 1,097 enfermos dados de alta del departamento de tuberculosis de un hospital público del condado, dentro de un período de 12 años, 122 salieron contrariando el consejo médico.
2. Las altas no aprobadas disminuyeron de 88 (24.3 por ciento) en los primeros seis años a 34 (9.5 por ciento) en los siguientes seis años.
3. Los casos con enfermedad abierta, fueron 42 (47.8 por ciento) de 88 en el primer grupo y 10 (29.4 por ciento) de 34 en el segundo grupo.
4. Las razones para este cambio favorable son:
   a) El desarrollo de un departamento activo incluyendo las actividades de la ciudad y del condado bajo un director a tiempo completo.
   b) Iniciación del cuidado a domicilio y abreviación de estancia en el hospital.
   c) Constante estado de alerta sobre tuberculosis fundamentalmente una enfermedad transmisible que requiere: íntima coordinación del hospital, el hogar, el cuidado médico, enfermería y servicios de salubridad.

RESUMÉ

1. Sur 1.097 malades sortis du service tuberculeux d'un hôpital public régional pendant une période de 12 ans, 122 quittèrent le service contre avis médical.
2. Les sorties irrégulières diminuèrent de 88 (24,3%) dans les six premières années à 34 (9,5%) dans les six autres années.
3. Les malades atteints de tuberculose avec expectoration bacillifère furent au nombre de 42 (47,8%) sur 88 dans le premier groupe, et de 10 (29,4%) sur 34 dans le second groupe.
4. Les raisons de cette modification favorable sont:
   a) le développment d'un service public sanitaire régional actif avec un directeur à temps plein;
   b) l'installation d'un plan de surveillance à domicile avec hospitalisation abrégée;
   c) le rappel constant que la tuberculose est assentiellement une affection contagieuse, demandant: la coordination étroite entre les services de l'hôpital, les services médicaux à domicile et les services publics d'hygiène.

ZUSAMMENFASSUNG

1. Von 1097 aus der Tuberkulose-Abteilung eines öffentlichen Kreiskrankenhauses innerhalt einer Zwölfjahresperiode entlassenen Patienten brachen 122 die stationäre Behandlung gegen ärztlichen Rat ab.
2. Entlassungen ohne ärztliche Zustimmung gingen von 88 (24,3%) während der ersten 6 Jahre zurück auf 34 (9,5%) während der zweiten 6 Jahresperiode.
3. Die offenen, infektiösen Patienten machten 42 (47,8%) von 88 in der ersten Gruppe und 10 (29,4%) von den 34 in der zweiten Gruppe aus.
4. Die Gründe für diesen Umschwung waren:
   a) Aufbau eines aktiven Stadt- und Land-Kreisgesundheitsamtes unter einem hauptamtlichen Leiter.
   b) Einführung eines Programmes für die häusliche Behandlung und Verkürzung des Krankenhausaufenthaltes.
   c) Ständiges Gewahtsein der Tuberkulose als einer in erster Linie übertragbaren Erkrankung, d.h. enge Zusammenarbeit zwischen Krankenhaus, häuslicher Pflege, ärztlicher Betreuung und dem öffentlichen Gesundheitsdienst.

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Cortisone and Irradiation*

II. Pulmonary Necrosis and Blood Vessel Impairment in Irradiated Cortisone-treated Rat Lung

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Introduction

In a previous study,[1] lung lesions were studied and discussed in both the irradiated noncortisone-treated and in the irradiated cortisone-treated rats. The histopathologic changes in the irradiated lung are well-known: Warren and Spencer,[2] Warren and Gates,[3] Hugeinin et al,[4] and more recently Berdjis and Brown[1] reported and described multiple cases in man and in animals.

Among the pharmacological agents directed at reducing secondary infection, inhibiting inflammatory response, and/or modifying the changes following irradiation, cortisone seems to respond with satisfaction.

In general, authors are more concerned about beneficial effect of cortisone than its possible harmfulness. Nevertheless, Cottier[5,6] reported pulmonary necrosis and pneumonia on the rats treated with large doses of cortisone. Berdjis and Brown[1] found also pulmonary necrosis, termed as liquefaction, in the animals treated with cortisone. These authors stated also that cortisone is a possible cause of frequent hyperemia and hemorrhage encountered in the lung parenchyma.

In the present investigation, cortisone was given to the irradiated and nonirradiated rats in order to study whether the pharmacological agent is responsible for necrosis, hemorrhage and vascular impairment found so frequently.

Material and Methods

Four groups of young adult, healthy rats were used in this experiment: Forty were given 3 mg. of cortisone acetate daily for a period of 100 days. From this group, 20 received a unique dose of 3000r x-ray irradiation on the chest three days after administration of cortisone. From the earlier experiments,[1] it was concluded that the action of cortisone was more efficient when it was given three days before irradiation rather than later. A third group of 20 untreated and nonirradiated rats served as controls. The fourth group (20 rats) received only one unique dose of 3000r on the chest. These animals were kept under observation and in separate cages for a period of 100 days approximately and were fed with standard laboratory diet. The conditions of irradiation were: 250 KV machine, 15 ma, 100 cm target distance, rate 65 r/min, filters Cu=.5 and Al=1 mm.

A few animals died during the experimentation and were carefully autopsied. They furnished interesting observations which will be discussed below. The remaining animals were sacrificed by the end of 100

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days and both lungs, the great vessels, and heart were fixed in 10 per cent formalin, embedded in paraffin and stained with routine hematoxylin and eosin, unless special mention is made. In this paper the changes in the lung and the pulmonary circulation were studied. The cardiovascular system will be studied elsewhere.[10]

Results

1. *Control Animals*: Apart from an occasional local epizootic pulmonary infection,[1,7] the lungs of the control rats showed no pathologic change (Figure 1a).

2. *Irradiated Lung of Noncortisone-treated Rats*: In brief, the irradiated lung showed patchy or lobular atelectasis with acute, subacute, or chronic inflammation, producing either pneumonitis, bronchopneumonia, bronchitis, or bronchiectasis with peribronchial and parenchymal abscesses. More or less extensive peribronchial, perivascular and alveolar fibrosis were present in all cases (Figure 1b). The bronchi were partly

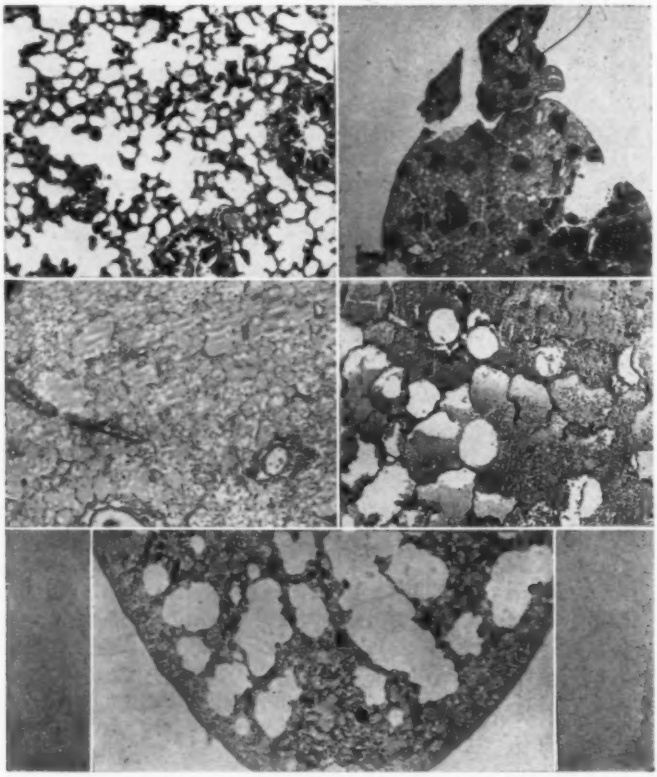

FIGURE 1: Representative photomicrograph sections of irradiated and nonirradiated cortisone-treated rat lung. H&E x 83 (a, c, d, e) and x 35 (b). *a*. Control untreated rat lung. *b*. Irradiated lung of noncortisone-treated rat, showing marked atelectasis, pulmonary infection with abscesses and extensive fibrosis. *c*. Irradiated lung of cortisone-treated rat exhibiting mass necrosis or liquefaction. *d*. Lung showing liquefaction, necrosis and hemorrhage. *e*. Nonirradiated lung of cortisone-treated rat illustrating the same changes as in "*d*" in addition to capillary thrombosis.

or entirely collapsed or obliterated disclosing partial resorption. As the result, there was foreign body giant cell reaction which increased the amount of fibrosis about the broncho-vascular trees.

3. *Irradiated Lung of Cortisone-treated Rat*: This condition described in detail elsewhere,[1] is summarized here: Atelectasis was partly or entirely replaced by "liquefaction" or necrosis, accompanied by hyperemia, stasis, intense congestion or hemorrhage (Figure 1c, 1d). Diffuse pulmonary hemorrhage also was frequently encountered in the animals which died during the experiment. Although the alveolar walls were

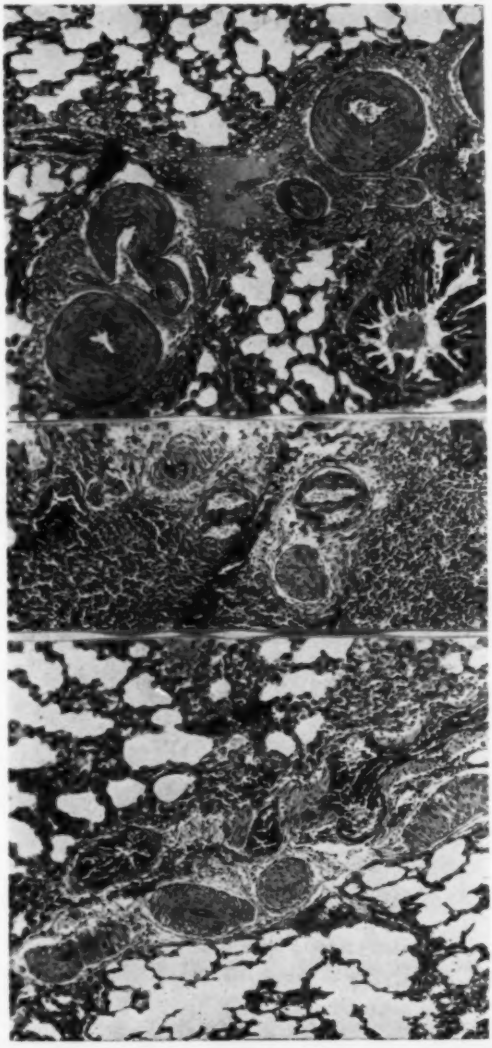

FIGURE 2 (a, b, c): Representative photomicrograph sections of impaired pulmonary blood vessels in cortisone-treated rat showing partly occluded prominent arteries with obvious thickening of the wall and narrowing of the lumen. H&E x 83.

thin and devoid of fibrosis, they were partially disrupted and disclosed degeneration. Whereas the amount of fibrosis and inflammatory cells was generally reduced, the lung parenchyma suffered from necrosis and hyperemia leading to frequent extravasation and/or hemorrhage (Figure 1d). Degenerative bronchial epithelium and desquamation were present in all cases. Peribronchial and perivascular lymphoid tissue was highly reduced. The wandering round cells of the alveolar walls were usually absent and the epithelial cells of the alveolar walls had undergone hydropic degeneration. The latter were partly or entirely destroyed. The remaining alveolar walls disclosed some obliterated capillaries.

4. *Nonirradiated Lung of Cortisone-treated Rat*: In order to find whether the lung parenchyma is damaged by cortisone, records were taken from the lungs of the animals which received cortisone alone. It was surprising to find that most of these lungs disclosed hyperemia, congestion, hemorrhage, and patchy atelectasis with multiple necrosis similar to that described previously as liquefaction (Figure 1d, 1e).

Furthermore, the alveolar walls exhibited also occluded capillaries while the small arteries showed evidence of narrowing lumen and thickening wall (Figure 2). The findings were similar to those described above (No. 3) under the topic "Irradiated Lung of Cortisone-treated Rat." The large branches of pulmonary artery, especially near and at the main trunk showed a thickened wall and a narrowing lumen. The media disclosed proliferation with foci of mucoid degeneration and/or calcification resembling Mönckeberg type arteriosclerosis (Figure 3). In some areas, there was cartilage formation and beginning of ossification (osteoblastic proliferation) with minute osteoid tissue.

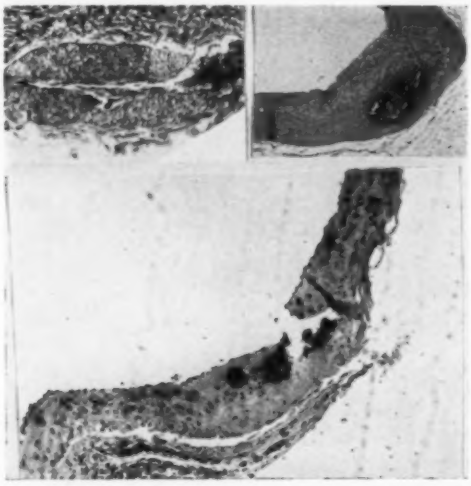

FIGURE 3 (a, b, c): Arteriosclerotic changes, Monckeberg type, in the main branches of pulmonary artery in the cortisone-treated rats. H&E x 83. (a, b, and c represent three stages of arterial changes).

Discussion

It has been shown that cortisone has a beneficial effect in the irradiated rat lung in preventing the occurrence of atelectasis.[1,3] Cortisone is also known to inhibit the inflammatory reaction and to reduce the amount of lymphoid tissue and the production of fibrosis. Berdjis and Brown[1] had analyzed this question in a previous study.

However, this so-called beneficial effect is more apparent than real, because cortisone seems to be responsible for liquefaction, necrosis, and blood vessel impairment. Many animals died during the experiment by c[illegible]e pulmonary hemorrhage and multiple pulmonary necrosis. Other animals sacrifi[illegible] moribund showed bilateral hemothorax, pulmonary necrosis, and hemorrhage. It is [illegible]re tentative than conclusive to say that cortisone is primarily a hemorrhagic agent p[illegible]se.

It seems that the mechanism of action of cortisone in the lung parenchyma is: (a) to increase the capillary pressure and its permeability, (b) to slow down the blood stream, and (c) to form a capillary thrombosis. Therefore before any capillary rupture occurs, there is accumulation of a large amount of serosity or sero-exudate fluid in the alveolar spaces, hence liquefaction. As the result, the alveolar walls are distended and disrupted showing large necrotic areas. This condition is referred to as liquefaction and necrosis by Berdjis and Brown[1] and by Cottier.[5,6]

The next stage is marked congestion, hyperemia, extravasation, and finally rupture of the capillary walls with occurrence of hemorrhage so frequently encountered in the lung parenchyma of the cortisone-treated rats. A few animals from both groups of irradiated cortisone-treated and noncortisone-treated died during the experiments. The cause of death appeared to be different in the cortisone-treated animals compared to those which were irradiated only. In the latter, the cause of death was primarily a massive pulmonary infection and atelectasis. The animals treated with cortisone died by hemorrhage without infection.

It can be said that cortisone affects the blood vessels in general leading to liquefaction, necrosis, and capillary thrombosis, or rupture. As the result of capillary impairment, there are some basic changes in the greater vessels leading to medial necrosis with calcification of the pulmonary artery and Mönckeberg type arteriosclerosis in its main branch. Irradiation alone does not affect the pulmonary artery. Liquefaction or capillary thrombosis were not observed in the irradiated animals. Some capillaries disclosed occlusion probably due to healing inflammatory process or overproduction of fibrosis. Berdjis[3] has analyzed the effects of irradiation alone on the cardiovascular system and found no evidence of pulmonary arteriosclerosis or blood vessel impairment in the lung parenchyma.

Conclusions

1. Irradiation reinforces the injurious effects of cortisone at the level of the lung parenchyma.
2. Whereas cortisone prevents pulmonary infection, it produces necrosis and/or liquefaction of the lung parenchyma (Figure 1).
3. Cortisone seems to act as a hemorrhagic agent per se.
4. Large daily doses of cortisone for a long time impairs the capillary function and produces arteriosclerotic lesions (Mönckeberg type). (Figure 3).

SUMMARY

In order to investigate the extent and nature of injury caused by cortisone in the lung parenchyma, 3 mgs of cortisone were given daily to irradiated and nonirradiated rats for a period of 100 days.

The cortisone-treated rats developed pulmonary hemorrhage and necrosis with liquefaction, which killed many animals during the experiments while irradiated animals died by pulmonary infection.

Although cortisone inhibits the inflammatory reaction and reduces the amount of lymphoid tissue and the production of fibrosis, it appears to be responsible for liquefaction, hemorrhage, and blood vessel impairment.

In general, it may be said that hyperemia, congestion, extravasation and/or hemorrhage, and capillary thrombosis occur in the lung parenchyma progressively. Liquefaction and/or necrosis are a result of increased capillary pressure and its permeability.

This blood vessel impairment leads to arteriosclerosis-like lesions (Mönckeberg type) in the main pulmonary artery.

RESUMEN

Para investigar la magnitud y la naturaleza del daño causado por la cortisona en el parénquima pulmonar, se dieron 3 mg. de cortisona diariamente a ratas irradiadas y no irradiadas por 100 días.

Las ratas tratadas con cortisona presentaron hemorragia pulmonar y necrosis con liquefacción, lo que mató a muchos animales irradiados muieron por infección pulmonar.

Aunque la cortisona inhibe la reacción inflamatoria y reduce la cantidad de tejido linfoide y la producción de fibrosis, parece que es responsable de la liquefacción, de la hemorragia y del daño vascular.

En general, puede decirse que la hiperhemia, la congestión, la extravasación y/o la hemorragia y trombosis capilar, ocurren progresivamente en el parénquima pulmonar. La liquefacción y/o la necrosis son el resultado de un aumento de la presión capilar y de su permeabilidad.

Este trastorno vascular conduce a lesiones semejantes a la arterioesclerosis (tipo Monckeberg) en la arteria pulmonar principal.

RESUMÉ

Pour évaluer l'étendue et la nature des altérations causées par la cortisone dans le parenchyme pulmonaire, 3 mmg. de cortisone furent donnés quotidiennement à des rats irradiés et non irradiés pendant une période de 100 jours.

Les rats traités à la cortisone furent atteints d'hémorragie pulmonaire et de nécrose avec liquéfaction, qui tuèrent beaucoup d'animaux pendant l'expérimentation, tandis que les animaux irradiés sans cortisone mouraient d'infection pulmonaire.

Bien que la cortisone inhibe la réaction inflammatoire et réduise le tissu lymphoïde et la production de fibrose, elle semble être responsable de la liquéfaction, de l'hémorragie, et de l'altération des vaisseaux sanguins.

En général, on peut dire que l'hyperémie, la congestion, l'extravasion associée ou non à l'hémmorragie, et la thrombose capillaire surviennent progressivement dans le parenchyme pulmonaire. La liquéfaction associée ou non à la nécrose est le résultat de l'augmentation de la pression capillaire et de sa perméabilité.

Cette altération vasculaire est cause de lésions à type d'artériosclérose (type de Mönckeberg) atteignant l'artère pulmonaire principale.

ZUSAMMENFASSUNG

Mit dem Ziel, das Ausmass und die Art der Schädigung zu erforschen, die das Lungenparenchym durch Cortison erleidet, erhielten bestrahlte und nichtbestrahlte Ratten 3 mg Cortison täglich 100 Tage lang.

Bei den mit Cortison behandelten Ratten entstand eine pulmonale Hämorrhagie und Nekrose mit Einschmelzung, die zum Tode vieler Tiere im Verlauf der Versuche führte, während die bestrahlten Tieren einer pulmonalen Infektion erlagen. Obwohl das Cortison die entzündliche Reaktion hemmt und die Ausdehnung des lymphoiden Gewebes und die Bildung der Fibrose verringert, scheint es doch verantwortlich zu sein für die Einschmelzung, Hemorrhagie und Gefasschädigung.

Im allgemeinen kann man sagen, dass die Hyperämie, Anschoppung extravasate und/oder Hämorrhagie und kapillare Thrombose im Lungenparenchym progressiv auftreten. Einschmelzung und/oder Nekrose sind das Resultat eines erhöhten Kapillardruckes und deren Permeabilität.

Diese Blutgefässchädigung führt in der grossen Lungenarterie zu Läsionen, die denen bei der Arteriosklerose ähnlich sind. (Mönckeberg Typ).

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Tuberculin Testing In Ontario Mental Hospitals

A 15-YEAR REVIEW OF STAFF

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Since 1937, the method used to protect the chest health of the staff in Ontario Hospitals has been to make x-ray film inspection of the chest and tuberculin test (Mantoux) of everyone on entering the service. All reactors have been re x-rayed annually, and all non reactors have had tuberculin tests repeated twice yearly. Tuberculin convertors are re x-rayed every three months for two years, then annually. Whenever a suspicious lesion was found, the person was referred to a sanatorium of his choice for further investigation. Similarly, if non-tuberculous lesions developed, the patient was referred to his physician. Films and report files are maintained permanently at the Ontario Hospital, Woodstock, and are always available to the physicians investigating any abnormal chest condition.[1-3] Recently, it has been decided to make x-ray film inspection of all staff personnel at every second annual chest survey. In addition to these measures, whenever an active or suspected case of tuberculosis was discovered in patient surveys, the patient was transferred to the Chest Diseases Division of Ontario Hospital, Woodstock, and all staff members and patients in contact with such were x-rayed every three months for one year and twice yearly the second year in addition to semi-annual tuberculin tests on those who were non-reactors.[4]

In 1943, the staff totalled 2,607. By 1957, the total was 6,979. The tuberculin tests are done by chest clinicians who visit each hospital twice yearly. The number of tests done, retests plus new staff, known reactors excluded, increased from 1,879 to 4,489, annually.

Table 1 shows the trend of reaction to tuberculin in this group, the reactors declining from about 74 to about 66 per cent.

The results of retesting non-reactors twice yearly is shown in Table 2. It may be noticed that men change reaction about twice as frequently as women, except for the years 1955-1957. In each of these years, an open case of tuberculosis in a patient remained undiagnosed for several months. In both groups, however, the rate of changed reactors has steadily declined from 58 to 23 per 1,000. In 1933-1935, C. A. Wicks[5] found the rate to be 219 per 1,000 in the same group.

Table 3 divides the tuberculin convertors into age groups and gives the rates per 1,000 for both men and women, 92 per cent of ages being traceable.

*From the Ontario Hospital.

TABLE 1 — REACTION—1943-1957

Year	Average No. of Staff	Average Negative Reactors	Per Cent Negative	Per Cent Positive
1943-45	2,698	718	26.6	73.4
1946-48	3,385	1,015	30.	70.
1949-51	3,977	1,260	31.7	68.3
1952-54	5,107	1,734	33.9	66.1
1955-57	6,519	2,231	34.2	65.8

TABLE 2 — TUBERCULIN CONVERTORS IN NON-REACTORS RETESTED

Year	Men			Women			Men and Women		
	No.	Con-vert	Per 1000	No.	Con-vert	Per 1000	No.	Con-vert	1000 Per
1943-1945	655	53	81	1500	72	48	2155	125	58
1946-1948	1200	59	49	1845	59	32	3045	118	38
1949-1951	1520	58	38	2269	48	21	3789	106	28
1952-1954	2037	101	50	3165	92	29	5202	193	37
1955-1957	2626	61	23	4368	99	23	6994	160	23
1943-1957	8038	332	41	13147	370	28	21185	702	33

The group under 20 is small because few staff begin employment under 20 years of age.

The group 60-69, is small because the majority by this time have become reactors. The retirement age of 65 also reduces the size of this group.

It will be noticed that there is a surprising uniformity in the four groups between 20 and 59. The steady decline in rate of changed reactors from 1943 to 1957 is seen, but only one age group has declined more than others which is the 60-69 group. The under 20 group shows a small but steady increase in rate of change.

These figures indicate that serial tuberculin testing is of great value in all age groups. A few years back, some of us thought that over the age of 25 or 30, tuberculin testing was not important.

As shown in Table 4, of the 702 changed reactors, 28 developed demonstrable lesions of which 19 developed demonstrable lesions during the first eight months. The overall rate is 40 per 1,000. In 1933-1935, C. A. Wicks[5] found this rate to be 74 per 1,000.

Table 5 shows the rates per 1,000 in age groups from 1943 to 1957 for convertors. There is, as expected, a wide variation between age groups

TABLE 3 — TUBERCULIN CONVERTORS IN AGE GROUPS
MEN AND WOMEN—RATE PER 1,000

		Under 20	20-29	30-39	40-49	50-59	60-69	All Ages
1943-45	No. Tested	100	550	575	580	290	51	2146
	Convertors	2	29	21	29	23	7	111
	Per 1,000	20	53	37	50	80	137	51
1946-48	No. Tested	140	780	815	825	410	63	3033
	Convertors	2	26	26	29	14	13	110
	Per 1,000	14	33	32	35	34	206	36
1949-51	No. Tested	174	967	1013	1025	510	90	3779
	Convertors	4	29	28	22	10	7	100
	Per 1,000	23	30	28	21	20	78	25
1952-54	No. Tested	240	1332	1394	1410	702	125	5203
	Convertors	9	51	49	46	19	4	178
	Per 1,000	38	38	35	33	27	32	34
1955-57	No. Tested	322	1790	1874	1895	944	168	6993
	Convertors	11	41	37	43	20	4	156
	Per 1,000	34	23	20	23	21	24	22
1943-57	No. Tested	976	5419	5671	5735	2856	497	21154
	Convertors	28	176	161	169	86	35	655
	Per 1,000	29	32	28	29	30	70	31

(92 Per Cent Traceable by Age)

TABLE 4 — TUBERCULIN CONVERTORS WHO DEVELOPED CLINICAL TUBERCULOSIS

	Men			Women			Men and Women				
	No.	Dev. Tbc.	Per 1000	No.	Dev. Tbc.	Per 1000	No.	Dev. Tbc.	Per 1000	Dev. Tbc.**	Per 1000
1943-45	53	0	0	72	6	83	125	6	48	4	32
1946-48	59	0	0	59	4	68	118	4	34	3	25
1949-51	58	2	34	48	5	104	106	7	66	3	28
1952-54	101	3	30	92	3	33	193	6	31	6	31
1955-57	61	3	49	99	2	20	160	5	31	3	19
1943-57	332	8	24	370	20	54	702	28	40	19	27

**Diagnosed directly following change in reaction.

and year periods; however, the figure of about 40 per 1,000 for all ages for 15 years is of some significance.

Ghon and others have demonstrated that everyone who becomes a reactor to tuberculin has lesions which are tuberculous even though most are too small to be demonstrated radiologically. For practical purposes, we have regarded those having demonstrable primary pulmonary infiltrates and those showing pleural involvement as clinical tuberculosis and have placed them immediately under treatment. The convertors without demonstrable infiltrates are kept under close observation and re x-rayed every three months for two years.

Table 6 shows the time in months after conversion that pulmonary or pleural lesions were demonstrable. It is seen that the majority occurred during the first few months after conversion. This shows the importance of immediate x-ray film inspection of all tuberculin convertors. Although miliary tuberculosis and meningitis are not common (we had no such cases), all tuberculin convertors are in some danger

TABLE 5 — TUBERCULIN CONVERTORS WHO DEVELOPED CLINICAL TUBERCULOSIS
Men and Women—Rate per 1,000 in Age Groups

		Under 20	20-29	30-39	40-49	50-59	60-69	All Ages
1943	Convertors	2	29	21	29	23	7	111
-	Dev. Tbc.	0	4	0	0	0	0	4
1945	Per 1,000	0	138	0	0	0	0	36
1946	Convertors	2	26	26	29	14	13	110
-	Dev. Tbc.	0	3	1	0	0	0	4
1948	Per 1,000	0	115	38	0	0	0	36.3
1949	Convertors	4	29	28	22	10	7	100
-	Dev. Tbc.	1	5	1	0	0	0	7
1951	Per 1,000	250	172	36	0	0	0	70
1952	Convertors	9	51	49	46	19	4	178
-	Dev. Tbc.	1	3	1	0	1	0	6
1954	Per 1,000	111	59	20	0	53	0	33.8
1955	Convertors	11	41	37	43	20	4	156
-	Dev. Tbc.	1	1	2	0	0	0	4
1957	Per 1,000	91	24	54	0	0	0	25.6
1943	Convertors	28	176	161	169	86	35	655
-	Dev. Tbc.	3	16	5	0	1	0	25
1957	Per 1,000	107	90.9	31	0	11.6	0	36.6

TABLE 6 — RADIOLOGICAL EVIDENCE OF TUBERCULOSIS
Time in Months after Converting

1 Mo.	2 Mo.	3 Mo.	4 Mo.	5 Mo.	6 Mo.	7 Mo.	8 Mo.	Over 8 Mo.
6	2	5	2	1	1	0	2	6

of developing this type of tuberculosis. Therefore, it is most important that close clinical observation as well as x-ray inspection be carried out for at least two years.

Of the 19 cases treated during this 15 year review, six were tuberculous pleurisy and the remainder were minimal pulmonary. The case rate for these is shown in the last two columns of Table 4.

At the present time, all changed reactors who developed tuberculosis have been treated and with the exception of the last two who were found in 1957 and are still under treatment, have become arrested and have returned to duty or other normal activity.

So far we have considered the tuberculin convertors from this group who have developed demonstrable lesions of tuberculosis. At the time of writing this article, there are about 160 staff members with pulmonary tuberculosis of whom about 12 are active, including the two from the changed reactor group.

The incidence of tuberculosis in this group has declined from 51 per 1,000 in 1943 to 23 in 1957 and a further decline may be expected. (figures for years in between are available) The majority of these are people who have had arrested tuberculosis for years. The number of such is rather high because employment in the mental hospital service is attractive for reasons of security, help in rehabilitation and protection by regular chest surveys. The incidence of active tuberculosis in 1957 was 171 per 100,000 which is close to the average of selected surveys by the Gage Institute for Metropolitan Toronto.

SUMMARY

The value of tuberculin testing for case finding in children and contacts has been stressed in recent years by Myers,[6] Heaf[7] and Hsu.[8] This 15-year review shows the value of serial tuberculin testing in an adult group who are not known contacts and are in apparent good health in the following ways:

Reactors are declining steadily.
The rate of tuberculin conversions is declining.
About 33 per 1,000 converted during the 15 years.
Men converted more often than women.
All age groups converted at about the same rate.
Of convertors about 31 per 1,000 progressed to active tuberculosis, approximately equally for men and women.
Convertors in age groups up to 39 years yielded the majority of active cases.
The majority of convertors becoming active did so within four or five months.
Cases of active tuberculosis where the tuberculin test was the first step in diagnosis showed an excellent prognosis.
The rate of staff members with arrested tuberculosis has steadily declined.

ACKNOWLEDGMENT: Acknowledgment is made to Dr. J. J. Weber, Superintendent, Ontario Hospital, Woodstock, for assistance in preparing this material.

Permission for publication has been kindly given by Dr. B. H. McNeel, Chief, Mental Health Division, Department of Health, Parliament Buildings, Toronto, Ontario.

RESUMEN

El valor de la reacción tuberculínica para descubrir los casos entre los niños y contactos ha sido recalcado en años recientes por Myers,[6] Heaf[7] y Hsu.[8]

Esta revisión de 15 años muestra el valor de las pruebas tuberculínicas en serie en un grupo de adultos que no son contactos conocidos y están en aparente buena salud, como sigue:

Los reactores decrecen constantemente.
Hay una declinación de la proporción de conversiones tuberculínicas.
Aproximadamente 33 por 1000 viraron la reacción durante los 15 años.
Los hombres viraron más a menudo que las mujeres.
De los que viraron su reacción aproximadamente 30 por ciento marcharon hacia la tuberculosis activa, aproximadamente de modo igual en hombres que en mujeres.
Aquéllos en el grupo de hasta 39 años de edad dieron la mayoría de casos activos.
La mayoría de los que viraron se hicieron activos dentro de 4 a 5 meses.
Los casos de tuberculosis activa en los que la reacción tuberculínica fué el primer paso para el diagnóstico, mostraron un pronóstico excelente.
La proporción de miembros del personal con tuberculosis detenida, ha declinado constantemente.

RESUMÉ

La valeur du test tuberculinique pour le dépistage chez les enfants, et pour la contagion a été mise en évidence dans les années récentes par Myers, Heaf, et Hsu. Cette revue portant sur 15 ans, montre la valeur des tests tuberculiniques en série, pratiqués chez un groupe adulte, qui n'a pas été en contact avec des tuberculeux et qui est en apparente bonne santé:
les individus réagissant à la tuberculine sont en diminution constante
le taux des virages à la tuberculine est en diminution
il y eut environ 33 virages pour mille pendant les quinze années;
les hommes firent leur virage plus souvent que les femmes;
dans les groupes de tout âge, les virages eurent lieu dans les mêmes proportions;
les individus ayant viré leur réactions au-dessus de 39 ans fournirent la majorité des cas de tuberculose active;
la majorité des individus ayant viré leurs réactions et qui furent atteints de tuberculose active le furent en moins de quatre à cinq mois après le virage;
les cas de tuberculose active dont le test tuberculinique fut le premier élément du diagnostic furent d'un excellent pronostic;
le taux des membres du personnel atteints de tuberculose inactive a constamment diminué.

ZUSAMMENFASSUNG

Auf die Bedeutung der Tuberkulinprüfung zur Ermittlung von Krankheitsfällen bei Kindern und Kontaktfällen wurde in jüngster Zeit von Myers,[6] Heaf[7] und Hsu[8] hingewiesen. Diese Übersicht über 15 Jahre zeigt den Wert von serienmässigen Tuberkulinproben an einer Gruppe von Erwachsenen, die keine bekannten Kontaktfälle waren und sich augenscheinlich bei guter Gesundheit befinden, auf folgende Weise:
Fälle mit positiver Reaktion nehmen ständig ab.
Das Verhältnis der Tuberkulin-Konversionen geht zurück.
Etwa 33 auf 1000 wurden während der 15 Jahre positiv.
Männer wurden öfter positiv als Frauen.
Alle Altersklassen konvertierten mit ungefähr der gleichen Häufigkeit.
Unter den Konvertoren kam es bei etwa 31 auf 1000 zur Entwicklung einer aktiven Tuberkulose, annähernd gleich oft bei Frauen und Männern.
Konvertoren in den Altersklassen bis zu 39 Jahren stellten die Mehrzahl der aktiven Fälle.
Die Mehrzahl der aktiv gewordenen Konvertoren wurden innerhalb von 4-5 Monaten aktiv.
Diejenigen Fälle von aktiver Tuberkulose, bei denen der Tuberkulintest den ersten Schritt zur Diagnose darstellte, hatten eine ausgezeichnete Prognose.
Die Anzahl der Angehörigen des Krankenhauspersonals mit ruhender Tuberkulose hat laufend abgenommen.

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Can Direct Vision Endoscopes be Autoclaved?

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The problem of bringing about desired change is one of the important objectives in education. New information through research is one of the methods used to convince people that they should change.

Chemical-disinfection research evaluations recommend that only those items that cannot be sterilized by heat should be disinfected by chemical methods.[1,2,3,4,5] A survey of the literature reveals that there is no effective chemical solution which will sterilize instruments in 30 minutes. The fastest acting germicide is irritating to tissues and must, therefore, be rinsed meticulously from the instruments. Considering the many pitfalls and limitations in using germicides, it seems that a more reliable method should be found. Autoclaving is the most rapid and reliable method of destroying micro-organisms.

It is held that some hospitals prepare their direct vision endoscopes with chemical solutions because some of the manufacturers of endoscopic instruments recommend that their instruments not be autoclaved.

Knowledge of the limitations of disinfectants and the recommendations of the instrument manufacturers caused the writers much concern. A set of direct vision endoscopes contaminated with tuberculosis organisms from one surgical patient with active tuberculosis required sterilization and use on another patient. The tubercle bacillus is not a spore-former, but the waxy coat which surrounds it makes it difficult to destroy. It is considered midway between spores and vegetative bacteria in its resistance to destruction. Processes of preparation should, therefore, be geared to destroy spore-forming micro-organisms.

Because the greatest concern was felt for the safety of the patient, it was elected to autoclave the instruments in spite of the manufacturer's recommendation to the contrary. Careful examination of the instruments following the sterilizing revealed no visible damage to the instruments or their accessories. Subsequently, in situations resembling the above conditions, it was elected to sterilize the instruments with steam under pressure.

Sufficient investigation of the autoclaving method has been completed to lead one to believe that this method can be employed to prepare direct vision endoscopes with complete safety for the patient and with only a minimal amount of damage to the endoscopes.

In connection with a research project for a master's thesis in 1955, the following tests were made.* A representative sample of endoscopic instruments was chosen from the supply cupboard. Care was taken to choose those instruments that were not used often so that the experimental instruments could be kept separate during the research project. The actual instruments tested are listed in Chart 1. Each separate piece of equipment was identified with a tag. The autoclaving and drying

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times and any special remarks were recorded on the tag during the research autoclaving period.

These instruments were autoclaved 101 times at 250° F. at 20 pounds of pressure, a total of 41 hours and 49 minutes and dried for a total of 19 hours and 38 minutes. It was attempted to autoclave them 20 minutes and dry them 10 minutes each time. The drying was effected by leaving the instruments in the autoclave with the steam in the jacket turned on and the autoclave door open slightly. The instruments and bulbs were examined and tested after each autoclaving period for the first 51 tests. They were examined and tested following every two autoclaving periods during the second fifty autoclaving tests.

The instruments were examined and tested for:

1. Evidence of damage to the surface of the metals — discoloration or etching,
2. Evidence of damage to the soldered joints,
3. Evidence of damage to the rubber cord — stickiness of rubber, separation between the rubber-metal joints, corrosion on light terminals and damage to the terminal collars,
4. Evidence of damage to the light carrier terminals and bulbs — the light bulbs were checked to see if they would carry current and light. No attempt was made to determine how long the bulbs would burn, and,
5. The atomizers were examined to determine if they would spray. It was felt that any internal damage that the instrument sustained would prevent them from spraying.

No attempt was made to clean the instruments until the research had been completed. The bronchalloy metal was easily returned to its original appearance. The brass metal was cleaned with metal polish and proved more difficult to return to its original appearance. There was no evidence of etching on the surface of the metal. A section of the brass endoscopes and atomizers was left unpolished so that interested people could examine the effect of the autoclaving periods and contrast the polished area with the discolored area and also with the surface of the instruments that had never been autoclaved.

The effects of the autoclaving are summarized in Charts 1 and 2.

Research Results

CHART 1

The following instruments were used in the research project and were autoclaved 101 times at 250° F. and 20 pounds of pressure. A total of 41 hours and 49 minutes and dried for a total of 19 hours and 38 minutes. The drying was affected by leaving the instruments in the autoclave with the steam in the jacket turned on and the autoclave door opened slightly. The instruments were autoclaved in an open instrument tray.

No attempt was made to clean the instruments until the research was completed. Some of the instruments were constructed from brass metal and some were made from bronchalloy metal.

The Following Results were Obtained:

Instrument	Effective of 101 Autoclavings	Effect of Cleaning
1. Esophagoscope #1 9 mm. x 53 cm. (brass)	Markedly discolored, but the surface remained smooth.	Discoloration was removed with metal polish.

CHART 1 (Continued)

2. Esophagoscope #2 9 mm. x 53 cm. (brass)	Same as above.	Same as above.
3. Esophagoscope #3 7 mm. x 30 cm. (bronchalloy)	No discoloration of metal. Surface remained smooth and bright, but had a few water marks.	The water marks were readily removed with a water-moistened cloth.
4. Esophagoscope #4 7 mm. x 30 cm. (bronchalloy)	Same as above.	Same as above.
5. Light Carriers (bronchalloy)	No evidence of discoloration. Surface remained smooth and bright.	None required, except to the contact terminal on occasion. (See observations).
Carrier #A (with E.S.I. lamp in place)	Lamp burned out on 95th autoclaving period. A total of 38 hours and 59 minutes autoclaving time and 18 hours and 58 minutes drying time. The replaced lamp lasted through the rest of the project.	
Carrier #B (with E.S.I. lamp out of carrier)	Lamp burned out on seventh autoclaving period. A total of 2 hours and 59 minutes autoclaving time and two hours and five minutes drying time. Replaced lamp lasted through the project.	
Carrier #C (with Pilling lamp in place)	Lamp burned out on 87th autoclaving period. A total of 35 hours and 54 minutes autoclaving time and 17 hours and 48 minutes drying time. The replaced lamp lasted through the rest of the project.	
Carrier #D (with Pilling lamp out of carrier)	Lamp burned out on 61st autoclaving period. A total of 25 hours and 39 minutes autoclaving time and 13 hours and 38 minutes drying time. The replaced lamp lasted through the rest of the project.	
6. Forceps globular objects 50 cm. (bronchalloy)	The bronchalloy parts unaffected. The blue tips showed a spotty color change and what appeared to be a small amount of corrosion. The surface of the blue tips remained smooth.	Corrosion easily removed with a water-moistened cloth.
7. Forceps globular objects 30 cm. (bronchalloy)	Showed some color change, but not as much as the above instrument.	Same as above.
8. Atomizer, Clerf 50 cm. (brass)	Surface discolored but remained smooth. Atomizer always sprayed, when tested, during the research project.	Discoloration removed with metal polish.
9. Atomizer, Clerf 30 cm. (brass)	Same as above. On the 51st autoclaving period, the glass-metal joint on the spray bottle separated.	Same as above.
10. Mirror, laryngeal angular, boilable Size #1 (chrome plate)	No discoloration of metal. Some water spots were present.	Water spots removed with a water-moistened cloth.

CHART 1 (Continued)

11. Mirror laryngeal angular, boilable Size #00 (chrome plate)	Same as above.	Same as above.
12. Cord, Jackson battery, #A black rubber with two black terminal sleeves	No apparent damage.	Required no cleaning.
#B black rubber	No apparent damage.	Same as above.
#C brown rubber cord, with one red and one black terminal sleeve	No apparent damage to the rubber, however, the *red* terminal sleeve developed small cracks.	Same as above.
#D brown rubber cord, with one red and one black terminal sleeve	Same as above.	Same as above.

CHART 2

OBSERVATION OF INSTRUMENTS FOLLOWING 101 AUTOCLAVING PERIODS

1. The bronchalloy instruments showed no evidence of discoloration. There were a few water marks left where droplets of steam evaporated during the drying process. These were easily removed with a water-moistened cloth.

2. The brass instruments were markedly discolored, but the surface remained smooth and there was no other apparent damage. This discoloration was removed with metal polish. After cleaning, they appeared to be the same as those instruments that had never been autoclaved.

3. The lighting systems revealed no evidence of damage other than those noted in Chart 1. The electrical terminals on the carriers, lamps, and cords seemed to be less affected by the number of autoclavings than by the nature of the load that was autoclaved just prior to them. When vaseline was autoclaved preceding the endoscopes, all of the terminals required cleaning with the Inperatori Cleaner.

4. The bronchoscopic forceps showed no evidence of being damaged except that the blue tips on the forceps showed spotty discoloration and a small amount of corrosion. The surface of the tip remained smooth. The corrosion was removed with a moistened cloth.

5. The Clerf Atomizers worked well throughout the research. The brass discolored as noted above. On the 51st autoclaving, one of the spray bottles separated between the glass-metal joint.

6. The cost of a Pilling-made Jackson Lamp is $2.15 . . . the same model manufactured by the E.S.I. Company is $1.48. The Pilling-made Clerf Bottle costs $1.75. (These prices were obtained from our supply department). Two Pilling lamps burned out. Two E.S.I. lamps burned out. One Clerf Bottle separated during the 101 autoclaving periods. This is a total cost of $9.01, or slightly less than $.09 per autoclaving period.

These data were circulated to 171 Veterans Administration hospitals in the United States. Ninety of the hospitals reported they were autoclaving all or part of their endoscopic equipment prior to receiving our research results. Forty-one of the hospitals reported they were using chemicals to prepare their instruments. Fourteen reported that endoscopic examinations were not performed in their surgery. Twenty-six failed to return the questionnaire. Twenty of the 41 hospitals using chemicals to prepare their endoscopes reported they switched to the autoclaving process after receiving our research results. Both of the hospitals where the authors work have used the autoclaving process for the three years that have elapsed since the original research project.

Approximately 522 endoscopic examinations have been completed at one hospital and 252 have been completed at the other, a total of 774 autoclaving periods, under our personal supervision.

The instruments present no further evidence of damage. It appears that the minor changes that occur in the instruments during the first few autoclaving periods, and as reported in the original research results, are all that can be expected to take place. The cost of instrument upkeep is minimal and the patient is safe from cross-contamination.

SUMMARY

The autoclaving method has been demonstrated to be effective and economical for preparing direct vision endoscopic instruments.

Bronchalloy is superior to brass when the autoclaving method is employed.

Black rubber cords appear to be superior to brown rubber cords because of the stronger black terminal collars.

There seems to be a weakness where cement is used between metal and glass.

From our experience, autoclaving is the method of choice for preparing direct vision endoscopes.

RESUMEN

Para preparar los instrumentos de visión directa endoscópica el autoclave ha demostrado ser económico y efectivo.

El Bronchalloy es mejor que el latón cuando se usa el método del autoclave.

Los cables con caucho negro parecen ser superiores a los que tienen caucho café a causa de las terminales negras son las fuertes.

Parece que hay alguna debilidad donde el cemento es empleado entre cristal y metal.

Según nuestra experiencia la esterilización al autoclave es el método preferible para preparar endoscopios de visión directa.

RESUMÉ

La méthode de l'autoclave s'est démontrée être efficace et économique pour préparer les instruments endoscopiques á vision directe.

Le "bronchalloy" est supérieur au cuivre lorsque la méthode de l'autoclave est utilisée.

Les raccords de caoutchouc noir semblent être supérieurs aux raccords de caoutchouc brun en raison de la plus grande résistance des colliers terminaux noirs.

L'utilisation du ciment entre métal et verre semble être une cause de moindre résistance.

D'après notre expérience, l'autoclave est la méthode de choix pour préparer les endoscopes á vision directe.

ZUSAMMENFASSUNG

Das Verfahren unter Verwendung des Autoklaven erwies sich als wirksam und wirtschaftlich bei der Vorbereitung der Instrumente für die direkte endoskopische Schau.

Bronchalloy ist dem Messing überlegen, wenn mit dem Autoklaven gearbeitet wird.

Leitungsschnüre aus schwarzem Gummi scheinen demjenigen aus braunem Gummi überlegen wegen der stärkeren schwarzen Endstücke.

An der Stelle, an der Zement zwischen Metall und Glas gebraucht wird, scheint sich eine schwache Stelle zu befinden.

Nach unseren Erfahrungen ist die Benutzung des Autoklaven die Methode der Wahl zur Vorbereitung des direkten endoskopischen Sehens.

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Pulmonary and Cardiac Function in Sickle Cell Lung Disease: Preliminary Report

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Physicians have long been intrigued by the unusual cardiac and pulmonary manifestations which may occur in patients with sickle cell anemia. Cardiomegaly, systolic and diastolic murmurs, recurrent bouts of pulmonary infiltration and chest pain, episodic or chronic dyspnea — all of these may appear in the sicklemic individual.

In recent years, considerable investigation has been carried out to define the anatomic and physiologic substrates upon which these fascinating clinical abnormalities are based. Such study has indicated that patients with sickle cell anemia have three major defects which may influence cardiopulmonary function: (1) a chronic and usually severe anemia; (2) an abnormal form of hemoglobin, designated as S hemoglobin; and (3) a tendency to develop multiple zones of pulmonary thrombosis. While each of these factors contributes to clinical disability, it is the occurrence of repeated pulmonary thromboses which may lead to the development of the interesting clinical entity which we have labeled "sickle cell lung disease."

Clinically, sickle cell lung disease parallels the well-known syndrome of multiple pulmonary emboli.[1,2] Characteristically, the symptoms and signs of thrombosis vary widely. Recurrent episodes of poorly-defined chest discomfort or frank, pleuritic chest pain may occur. Fever and some dyspnea are common with these episodes, although hemoptysis is rare. Small infiltrations which heal by linear scarring may appear on serial chest roentgenograms (Fig. 1). A variable degree of leucocytosis may occur. In our experience, the search for pathogens in the sputum is usually unrewarding. Furthermore, resolution of the fever, leucocytosis and roentgenographic abnormalities occur in the same time-period whether or not antibiotic therapy is instituted. These thrombotic episodes are usually diagnosed as "pneumonitis" or non-specific manifestations of sickle cell "crisis."[1]

Occasionally, in patients who have experienced this syndrome repeatedly, evidence suggesting residual cardiopulmonary disease appears in the form of excessive fatigue, dyspnea with mild exercise and cardiac enlargement especially of the right ventricular type. Cyanosis is rarely seen, however, probably because of the severity of the anemia.

Microscopic sections of the lung indicate that sickle thrombi occur chiefly in the pulmonary capillaries and smaller arterioles (Figs. 2, 3). If widespread obstruction has occurred, right ventricular enlargement may be found at direct examination.[3-5]

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Presented in part at the 24th Annual Meeting, American College of Chest Physicians, San Francisco, California, June, 1958.

This investigation was supported by PHS Research Grant H-3807 from the National Heart Institute, Public Health Service.

These clinical and pathological observations suggest that thrombotic obstruction in the pulmonary vascular bed is not uncommon in sickle cell subjects. However, two major unknowns exist regarding the process: (1) why do these thromboses occur; and (2) what are the cardiopulmonary consequences of these occlusions?

In order to answer these questions, combined cardiac catheterization and pulmonary function study was carried out in ten patients with electrophoretically-pure S hemoglobin.* The technique and procedure of these studies has been described elsewhere.[4] The data acquired from this small group permit us to make some preliminary comments upon both the causes and the consequences of thrombotic sickle cell lung disease.

Mechanisms of Pulmonary Thrombosis in Sickle Cell Subjects

At the present time, it appears that thrombosis in the pulmonary vasculature of these patients is a consequence of simple obstruction of the smaller pulmonary vessels by sickled red blood cells. The capillaries and terminal arterioles of the lung are of such calibre as to enforce

*We are indebted to the Hematology Sections of the Georgetown and George Washington University Services of the D. C. General Hospital for obtaining the electrophoretic hemoglobin patterns in these patients.

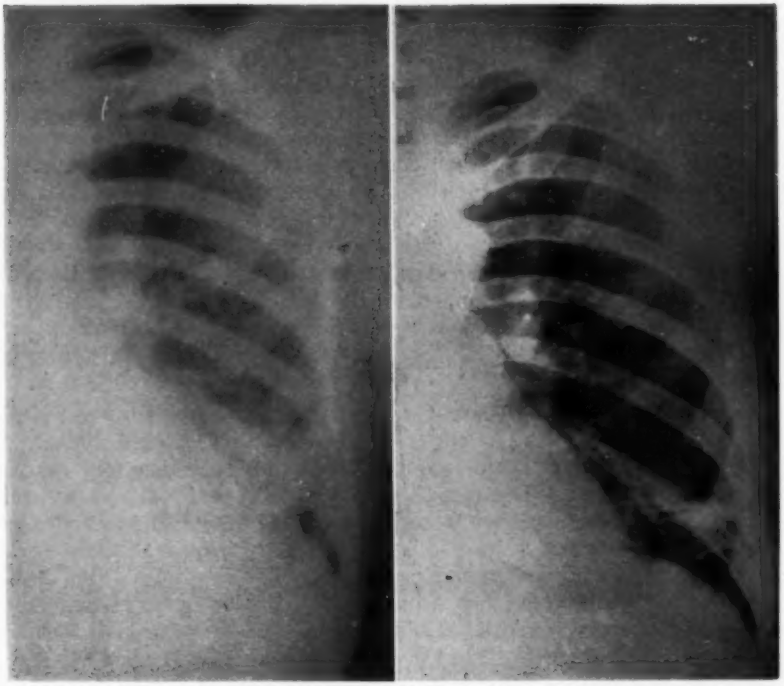

FIGURE 1: Chest roentgenograms of a 28 year old colored man with sickle cell anemia who entered the hospital with fever and pleuritic left chest pain. At the left is roentgenogram on admission showing wedge-shaped infiltrate at the left base. On the right is roentgenogram two weeks after admission showing linear healing characteristic of pulmonary infarction.

"single file" passage upon the normal red cell. If cells containing S hemoglobin have assumed bizarre shapes prior to entering these small vessels, mechanical obstruction would appear a likely consequence. Should even partial obstruction develop, the associated stagnation of flow might well be sufficient to administer the thrombotic *coup-de-grace*.

Presumably, then, a key factor in sickle thrombosis in the lung is the presence of a great percentage of sickled red cells in blood reaching the lungs. Therefore, in searching for the mechanisms of thrombosis, attention should be directed toward those factors which may potentiate sickling in the venous blood.

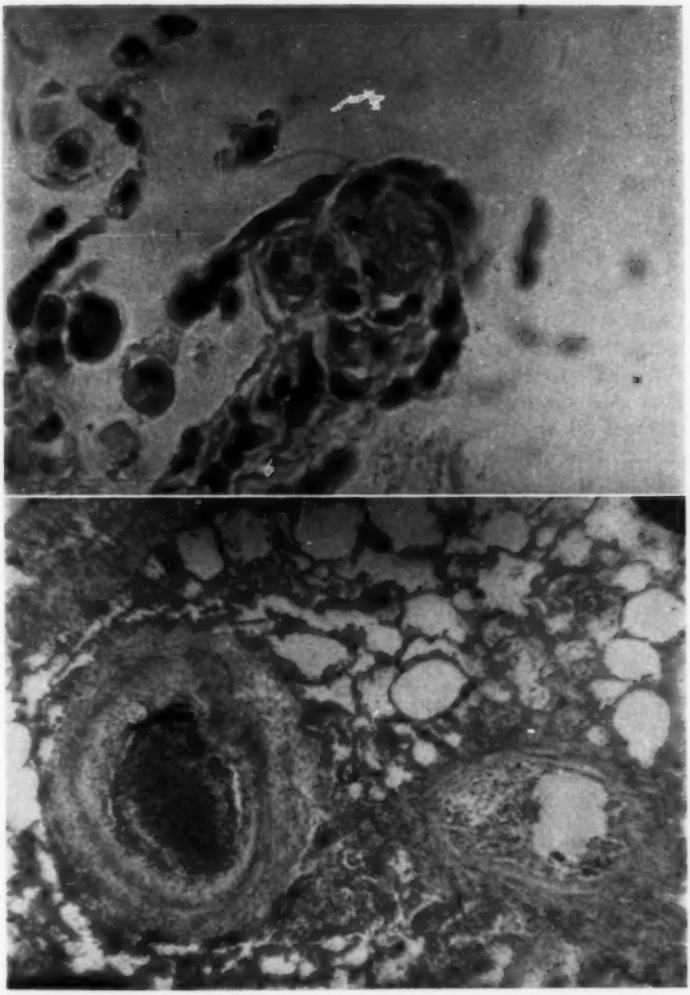

FIGURE 2: Microscopic section from lung of 29 year old colored man with sickle cell anemia who succumbed after multiple admissions for pulmonary infarction and progressive right ventricular failure. Section demonstrates thrombosed pulmonary capillary. (x44). FIGURE 3: Microscopic section of lung from same patient as Figure 2 showing thrombosed pulmonary arteriole. (x3.5).

Since exposure of susceptible cells to *low oxygen tensions* is a potent method for inducing the sickling phenomenon,[9,10] low venous oxygen concentrations may be expected to produce intense sickling of the red cells entering the lungs. That this mechanism may be operative *in vivo* is suggested by our experimental data which indicate that low venous oxygen values are common in patients with sickle cell anemia. When the saturation of the mixed venous blood of these patients is compared with the expected saturation according to the oxygen uptake (VO_2), these values are almost uniformly below normal or at the lower limits of normal (Fig. 4). The average mixed venous saturation was 59.8 per cent at rest and decreased to 43.9 per cent with exercise. At such low oxygen concentrations, a high degree of sickling might be expected among red cells reaching the pulmonary bed.

The obvious question posed by these findings is, "Why do these patients have this unfortunate tendency toward low oxygen saturation of the mixed venous blood?" While this question cannot be answered with precision at the present time, it appears that at least three independent factors may play a part in producing this abnormality (Fig. 5). First, several investigators[7,8] have indicated that the oxyhemoglobin dissociation curve for sickle (S) hemoglobin lies to the right of that for normal (A) hemoglobin. This shift means that a given oxygen tension will not saturate S hemoglobin as fully as normal hemoglobin would be saturated. Conversely, when oxygen tensions and saturations are both measured in these patients, the presence of S hemoglobin should lead to oxygen tensions consistently in excess of those predicted from saturation values using the oxyhemoglobin dissociation curve for normal hemoglobin. This situation is confirmed by our experimental data, though an unexplained patient variability does exist (Fig. 6). In view of this behavior of S hemoglobin, sickle patients have a "built in" de-

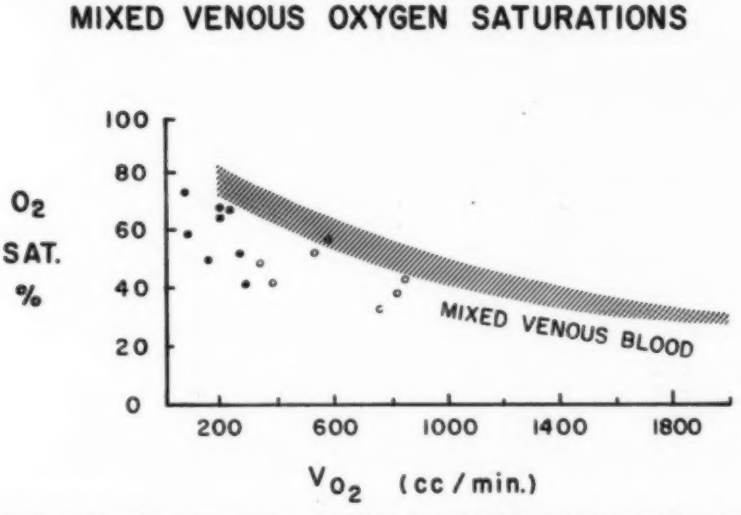

FIGURE 4: Mixed venous oxygen saturations in sicklemic subjects at various levels of oxygen uptake. Normal range is indicated by hatched area. Closed circles are resting values; open circles are exercise values.

gree of arterial and venous desaturation, for red cells containing this hemoglobin will leave the pulmonary capillary with below-normal saturation despite exposure to normal alveolar oxygen tensions.

By itself, this defect in S hemoglobin would not produce severe desaturation of the venous blood. Unfortunately, most of these subjects also have a marked anemia. Hemoglobin values in our patients were extremely low, averaging 7.3 gms per cent. This degree of anemia can be responsible for an additional lowering of the venous saturation. When low hemoglobin concentrations exist in the blood, tissues must extract a larger proportion of the available oxygen from red cells as they pass through the peripheral capillary bed.[11-13] This adaptive phenomenon in anemia results in an abnormally low saturation of the mixed venous blood. When anemic subjects exercise, the per cent peripheral utilization may be quite high and extremely low levels of venous saturation may be reached.

In addition to the presence of S hemoglobin and anemia, a third factor may contribute to abnormally low venous saturations in these patients. As will be indicated in greater detail below, those sickle subjects who have suffered widespread pulmonary thrombi may develop a diffusion insufficiency for oxygen in the lung.[8] This defect also leads to incomplete saturation of the blood leaving the lungs, and, thereby, exaggerates venous desaturation.

While exposure to low oxygen tensions is regarded as a dominant influence, exposure of red cells to acid pH and heat also potentiates sickling.[9,10] Increased venous acidity may appear if the peripheral oxygen

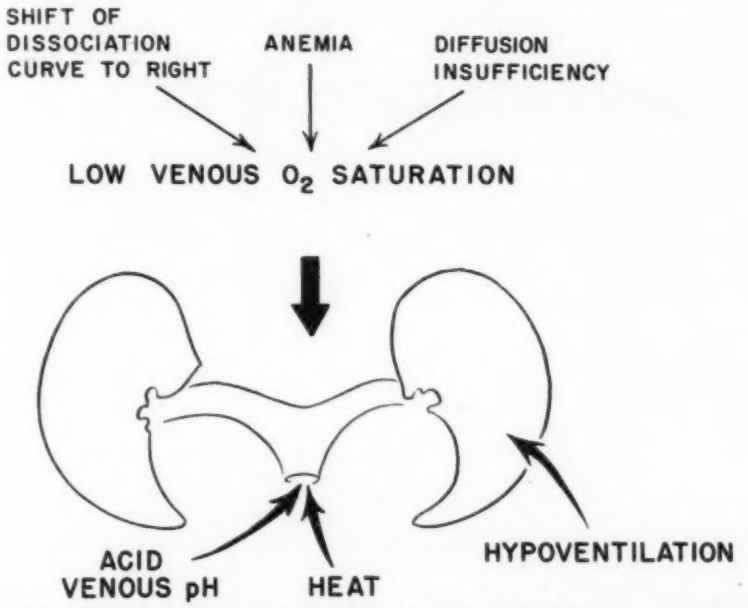

FIGURE 5: Diagrammatic representation of the potentiators of the sickling phenomenon.

lack in anemia forces cells to utilize anaerobic metabolic pathways which release acid end-products. Increased temperature of the venous blood may occur with the fever of sickle "crises."

Finally, in this analysis of factors inducing sickle cell pulmonary thrombosis, it should be recalled that a certain portion of the pulmonary blood flow normally perfuses poorly-ventilated alveoli.[14] This "physiologic shunting" contributes to arterial and venous desaturation. More important, however, is the fact that arteriolar constriction may develop in such hypoventilated areas.[15] This constriction would render vessels especially vulnerable to plugging by sickled cells.

Cardiopulmonary Consequences of Pulmonary Thrombosis

The anatomic defect imposed by widespread thrombotic events is a decrease in available "capacity" of the pulmonary vascular bed. Such anatomic diminution is significant because the low-pressure, low-resistance hemodynamics of the pulmonary circulation are dependent upon the tremendous reserve capacity of this vascular bed. This reserve permits the pulmonary vascular bed to accept large increases in blood flow with minimal increases in pulmonary arterial pressure or right ventricular work.[16] Thus, preservation of normal hemodynamics is accomplished by "opening" new vascular capacity in the lung. The chain

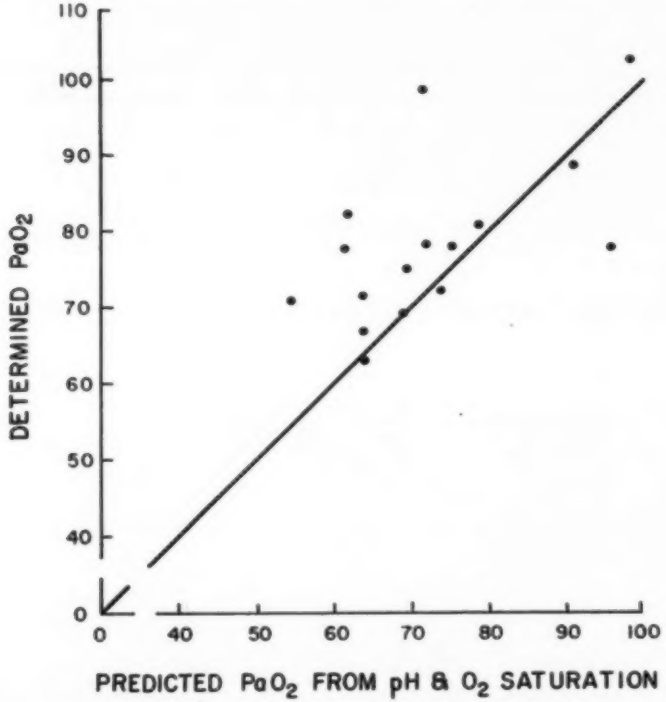

FIGURE 6: Relationship of the measured arterial oxygen tensions in sicklemic subjects to the tensions predicted from pH and oxygen saturation using the oxyhemoglobin dissociation curve for normal (A) hemoglobin. Solid line indicates expected relationship.

of events by which pulmonary arterial pressure and right ventricular work escape abnormal elevations may be expressed in another way; viz., the normal individual is able to lower the calculated "pulmonary vascular resistance" as pulmonary blood flow is increased.[15,16]

Pulmonary thrombotic disease decreases this vital reserve capacity of the pulmonary vascular bed. Fortunately, the unused reserve is so vast that considerable thrombotic obstruction must occur before hemodynamic abnormalities appear. However, if thromboses are sufficiently widespread, the expandable reserve is depleted. Resistance in the pulmonary circuit then becomes fixed. When this fixation occurs, any increase in the pulmonary blood flow can be achieved only at the expense of an abnormal increase in both the pulmonary artery pressure and the work of the right ventricle.

Severe reduction of the pulmonary vascular bed results in an increased *velocity* of blood flow through the remaining vessels. Normally, venous blood achieves virtually full equilibration with alveolar oxygen tension during its transit through the alveolar capillary. End-capillary and alveolar oxygen tensions are therefore almost identical. While addition of the "venous admixture" does lead to a slightly lower oxygen tension in the arterial blood, the difference between alveolar and arterial oxygen tensions normally is quite small (below 20 mm Hg). Therefore, at normal flow rates, there is a small difference, or gradient, between the oxygen tension of arterial blood and that present in alveolar gas. This difference is referred to as the alveolo-arterial (or A-a) oxygen tension gradient.

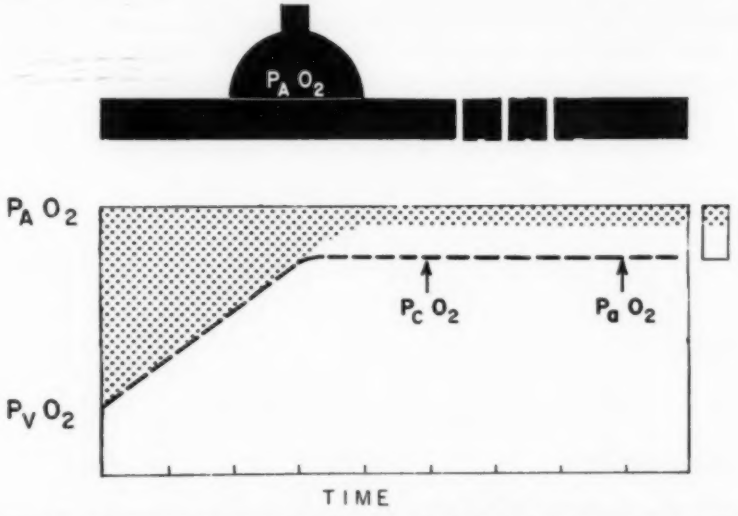

FIGURE 7: Diagrammatic representation of effect exerted by excessive velocity of capillary blood flow in a depleted pulmonary vascular bed. Dotted area shows normal change from venous oxygen tension (P_VO_2) to end-capillary (P_cO_2) and arterial (P_aO_2) oxygen tensions as blood passes alveolus. Dotted portion of box at right shows "normal" gradient between alveolar (P_AO_2) and arterial oxygen tensions. Dashed line shows failure of equilibration which occurs when "contact time" is decreased. The A-a gradient increases, as indicated by the whole box at right. The effect of venous admixture is not indicated.

If large areas of the pulmonary capillary bed are obstructed, blood may flow through the remaining capillaries with extreme speed. The time of contact between capillary blood and alveolar gas is reduced. If this accelaration of velocity reaches a critical level, flow through the pulmonary capillaries may become so rapid that blood leaves contact with alveolar gas before normal oxygen tension can be achieved. This produces an abnormal gradient between alveolar and end-capillary oxygen tensions (Fig. 7). This failure of equilibration is reflected as an abnormally-wide gradient between alveolar and arterial oxygen tensions, i.e., a widened "A-a gradient." The term "diffusion insufficiency for oxygen" is used to describe this failure of oxygen equilibration in the lung. Therefore, the wide A-a gradient of diffusion insufficiency is another indication of severe capillary bed depletion.

The total pattern of abnormalities which may be expected in patients who have suffered extensive obstruction (or destruction) of pulmonary vessels by sickle thrombi (or by any other mechanism) may be summarized as follows: The primary anatomic defect is a diminution of available capillary bed area. This leads to the twin physiologic defects of fixed pulmonary vascular resistance and increased velocity of blood flow. Depending on the level of pulmonary blood flow, these defects may produce a variable degree of diffusion insufficiency (with widening of the A-a gradient), pulmonary hypertension and increased right ventricular work.

With minimal vascular obstruction, these abnormalities are absent. With moderately extensive damage, the aberrations are manifested only when pulmonary blood flow is increased, as by exercise. If severe loss of cross-sectional area has occurred, these defects are present at rest and exaggerated by exercise. Because their anemia is associated with abnormally high pulmonary blood flows,[13] sickle subjects should develop these abnormalities at less marked degrees of pulmonary vascular compromise than the normal individual. In our series, resting blood

M.L. 19 CF S-S HGB.

	N	REST	EXERCISE
Q (L./min.)		4.7	10.9
P.A.R. (dynes sec cm^{-5})	<200	160.0	145.0
PAm (mm Hg)	<20	17.0	30.5
A−a gradient (mm Hg)	<20	34.0	43.0
R.V.W. (mkg/min.)	<1.0	0.5	3.0

FIGURE 8: Representative cardiopulmonary data from a 19 year old sicklemic subject with pulmonary vascular compromise. (See Text).

flows averaged 4.4 L./min./m² and increased to an average of 8.7 L./min./m² with exercise.

Of the 10 patients studied, three demonstrated the pattern which suggests moderate to severe pulmonary vascular obstruction. Representative data from one of these patients is shown in Figure 8. At rest, with a pulmonary blood flow of 4.7 L./min., no striking abnormality is present, although the A-a gradient is somewhat widened. However, during exercise, several pathologic responses of the pulmonary bed are apparent. Despite an increase in pulmonary blood flow to 10.9 L./min., the pulmonary arteriolar resistance remained virtually fixed, failing to show the expected decline. The mean pulmonary arterial pressure rose to an abnormal value of 30.5 mm Hg., and the right ventricular work increased six-fold. Furthermore, the A-a gradient widened to a distinctly abnormal value of 43 mm Hg.

Since almost two-thirds of the pulmonary bed must be obliterated before abnormalities of this severity appear, it is not surprising that such patients are not common. However, data obtained during exercise suggests that a number of patients may have a milder degree of pulmonary vascular compromise (Fig. 9). In eight patients, the pulmonary arterial pressure rose during exercise. In six cases, it equalled or exceeded the high normal value of 20 mm Hg. Changes in A-a gradient were also conspicuous. If 20 mm Hg is taken as a generous upper-limit-of-normal, abnormalities of the A-a gradient were frequent at rest. With exercise, seven patients showed further widening of this gradient. Thus, these findings suggest that other patients in this group may have a degree of

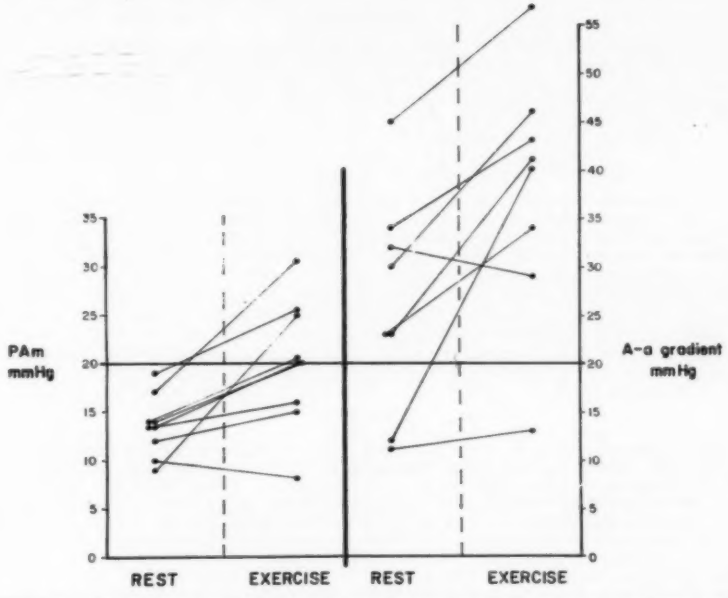

FIGURE 9: Changes in pulmonary arterial mean pressure and A-a oxygen tension gradient in sicklemic subjects with exercise. (Pressure measurments in one patient and gradient determinations in two were incomplete or unsatisfactory).

pulmonary vascular compromise which is not apparent at rest, but becomes detectable when pulmonary blood flow is raised by exercise.

Comments

The clinical observations indicating that pulmonary thrombosis is a frequent complication in individuals with "pure S" hemoglobin[1] assume greater significance in the light of the data presented here. It is apparent that considerable hemodynamic aberration may result from these small, repeated insults to the pulmonary vascular bed. One patient in this series succumbed, at age 29, after repeated hospital admissions during which evidence of pulmonary infarction and progressive right ventricular failure were the dominant features.[2] At autopsy, fresh and old thrombotic occlusion was rampant throughout the smaller arterioles and the capillaries of the pulmonary vascular bed (Figs. 2, 3). A dilated pulmonary artery, hypertrophied and dilated right ventricle and evidence of passive congestion of the viscera were present. In another case in which autopsy was performed, pulmonary vascular thrombosis was considerably less widespread, and minimal right ventricular hypertrophy was present.

There is obviously a marked variation in the extent to which various "S-S" subjects occlude the pulmonary vascular bed. While age may play some role, it is not the only factor, since one of the most severely affected patients in this series was only 19 years old. Perhaps the extent of concurrent hemolysis of red cells may play a crucial role, since evidence recently has appeared indicating the thrombogenic potential of red cell stroma.[17] Other events, such as transitory hypoventilation in small pulmonary segments due to bronchitis or pneumonitis, may be sufficient to encourage thrombosis in sickle subjects, while they would be of little significance in the normal individual.

It is apparent that elucidation of those factors which influence the extent, frequency and, possibly, the duration of pulmonary thrombosis in these patients poses a challenge requiring further study. This challenge must be met if therapeutic devices are to be developed which can alter the prognosis of sickle cell subjects. At the present time, avoidance of extremes of exertion, especially during periods of marked anemia, and perhaps administration of alkali in the acute situation[10] are the only therapeutic suggestions which can be offered. Anticoagulation, in our experience, has proved of questionable benefit, as might be expected in view of the probable "mechanical" pathogenesis of sickle thrombosis. It appears that real therapeutic advance will await the development of techniques whereby cells containing S hemoglobin can be induced to retain a normal contour.

SUMMARY

(1) Pulmonary thrombosis in sickle subjects appears to be a consequence of mechanical obstruction of small pulmonary vessels by sickled cells. Such cells may gain entrance into the pulmonary vascular bed in high concentration because of abnormally low oxygen concentrations in the venous blood. This desaturation is the end-result of several independent factors. Fever and an acid pH of venous blood also may potentiate sickling. Vessels in hypoventilated areas of the lung may constrict under the influence of abnormal alveolar oxygen and carbon dioxide tensions, rendering them especially susceptible to thrombotic occlusion by the sickled cells.

(2) If thrombotic events involve a large area of the pulmonary vascular bed, cardiopulmonary abnormalities may develop. These include fixation of pulmonary vascular resistance, pulmonary hypertension, increased right ventricular work and diffusion insufficiency for oxygen. The high cardiac output imposed by anemia in these patients tends to exaggerate these abnormalities. However, the extent of vascular loss may become apparent only when the pulmonary blood flow is raised, as by exercise.

(3) The variability in extent of pulmonary thrombotic involvement among patients with S-S hemoglobin remains unexplained, though a number of possibilities exist.

(4) Effective prophylaxis and therapy in these patients awaits the discovery of satisfactory methods for preventing or reversing the sickling phenomenon *in vivo*.

RESUMEN

1. La trombosis pulmonar en los sujetos con el fenómeno de las celdillas en hoz (sickled cells) parece ser una consecuencia de la obstrucción mecánica de los pequeños vasos pulmonares por las celdillas con ese fenómeno. Tales celdillas pueden lograr acceso dentro del lecho capilar pulmonar en elevada concentración a causa de las bajas concentraciones anormales en la sangre venosa. Esta desaturación es el resultado final de varios factores independientes. La fiebre y un pH ácido de la sangre venosa, puede también potenciar el fenómeno. Los vasos en las áreas hipoventiladas del pulmón se pueden estrechar bajo la influencia del oxígeno alveolar anormal y de las tensiones de bióxido de carbono haciéndolos especialmente susceptibles a la oclusión trombótica por esas celdillas en hoz.

2. Si la trombosis compromete un área grande del lecho vascular pulmonar, pueden desarrollarse anomalías cardiopulmonares. Estas incluyen la fijación de la resistencia

vascular pulmonar, la hipertensión pulmonar, el aumento del trabajo del ventrículo derecho y la insuficiencia de difusión del oxígeno. El elevado rendimiento cardiaco impuesto por la anemia en estos enfermos, tiende a exagerar las anormalidades. Sin embargo, la extensión de la pérdida vascular puede hacerse aparente sólo cuando el flujo pulmonar sanguíneo aumenta como en el ejercicio.

3. La variabilidad en la extensión del compromiso trombótico pulmonar entre los enfermos con hemoglobina S-s, permanece inexplicada, aunque cierto número de posibilidades existe.

4. La profilaxis efectiva y el tratamiento de estos enfermos está en espera del descubrimiento de métodos efectivos para evitar u obtener la reversión del fenómeno de celdillas en hoz *in vivo*.

RESUMÉ

1. La thrombose pulmonaire chez les sujets atteints de drépanocytose semble être la conséquence d'une obstruction mécanique des petits vaisseaux par des cellules falciformes. De telles cellules peuvent pénétrer danes le lit vasculaire pulmonaire à haute concentration à cause de la concentration d'oxygène anormalement basse dans le sang veineux. Cette désaturation est le résultat final de plusieurs facteurs indépendants. La fièvre et le pH acide du sang veineux peuvent également augmenter la drépanocytose. Les vaisseaux dans les zones hypoventilées des poumons peuvent se contracter sous l'influence de tensions alvéolaires anormales en oxygène et en gaz carbonique, les rendant particulièrement aptes à l'occlusion thrombotique par les cellules anormales.

2. Si des faits produits par la thrombose atteignent une large zone du lit pulmonaire vasculaire, des anomalies cardiovasculaires peuvent se développer. Celles-ci comprennent la fixation de la résistance vasculaire pulmonaire, l'hypertension pulmonaire, l'augmentation du travail du ventricule droit, et une insuffisance de diffusion de l'oxygène. Le haut débit cardiaque imposé par l'anémie chez malades tend à exagérer ces anomalies. Cependant, l'importance de la perte vasculaire ne peut devenir apparente que lorsque le débit sanguin pulmonaire est augmenté, par exemple à l'occasion de l'exercice.

3. La variabilité de l'extension de l'atteinte pulmonaire thrombotique parmi les malades avec hémoglobine S reste inexpliquée, bien qu'un grand nombre de possibilités existent.

4. La prophylaxie et le traitement efficaces chez ces malades ne seront possibles que le jour où l'on aura découvert des méthodes satisfaisantes pour prévenir ou guérir le phénomène *in vivo*.

ZUSAMMENFASSUNG

1. Eine pulmonale Thrombose bei Patienten mit Sichelzell Erkrankung dürfte eine Folge des mechanischen Verschlusses der kleinen Lungengefäße durch Sichelzellen sein. Solche Zellen können in das pulmonale Gefäßbett in hoher Konzentration Zutritt finden als Folge einer abnorm niedrigen Sauerstoffkonzentration im venösen Blut. Diese Entsättigung ist das Resultat verschiedener selbständiger Faktoren. Fieber und ein saüren pH wert des venösen Blü können das Auftreten von Sichelzelken im Blut erheblich verstärken. Gefäßein mangelhaft ventilierten Lungenabschnitten können sich unter dem Einfluß abnormaler alveolerer Sauerstoff und C_{O2}— Spannungen kontrahieren und machen sie so in besonderem Maße empfänglich für einen thrombotischen Verschluß durch die Sichelzellen.

2. Betrifft ein thrombotisches Geschehen einen großen Bereich des pulmonalen Gefäßbettes, so können daraus kardiopulmonale Veränderungen entstehen. Hier-hin gehören die Fixationen des pulmonalen Gefäßwiderstandes, pulmonaler Hochdruck, erhöhte Belastung des rechten Herzens und Insuffizienz der Sauerstoffdiffusion. Das durch die Anaemie bewirkte große Herzminutenvolumen führt bei diesen Kranken dazu, diese Veränderungen noch zu verstärken. Es kann jedoch so sein, daß das Ausmaß des Gefäßverlustes nur in Erscheinung tritt, wenn sich die pulmonale Durchströmung verstärkt, etwa bei Belastung.

3. Für die Verschiedenheit im Ausmaß der pulmonalen thrombotischen Veränderungen bei Kranken mit Sichelzell-Haemoglobin fehlt noch immer eine Erklärung, obwohl eine Anzahl von Möglichkeiten hierzu bekannt ist.

4. Eine effektive Prophylaxe und Therapie bei diesen Kranken sieht noch de-r Entwicklung befriedigender Methoden zur Verhütung oder Beseitigung des Sichelzellphänomens *beim Lebenden* entgegen.

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The Influence of Pregnancy and Delivery on Pulmonary Tuberculosis

(Clinical observations on pregnancies observed in tuberculous patients at the Malben Hospital for Chest Diseases, in the years 1952-1957).

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The problem of the influence of pregnancy on pulmonary tuberculosis has for many years engaged the attention of lung specialists, as well as that of obstetricians. Judging from the numerous recent studies on this subject, great importance is attached to this problem even today.

In the last century, tuberculosis cases discovered during pregnancy reached 0.5 per cent (Cooper). With the introduction of routine fluoroscopy during pregnancy, discovered tuberculosis cases rose, and reached 1.5 per cent to 2 per cent (Giselle). According to a report by Schaefer, covering the years 1952-1957, i.e., since the beginning of the antimicrobial era, there was no change in the incidence of tuberculosis complicating pregnancy. This shows that the tuberculosis-pregnancy problem is still acute.

Until the middle of the 18th century, it was believed that pregnancy, and particularly delivery, were beneficial to the tuberculous process. Little by little, the majority of authors and research workers modified this point of view and became convinced that pregnancy and delivery were detrimental to tuberculosis. The number of abortions for tuberculosis increased to such proportions that in 1923, Rist, Pankow and others declared that it was necessary to interrupt a pregnancy in every case of active tuberculosis, so as to prevent exacerbation of the disease after delivery.

This was the common concept until 1950. In a survey of 120 deliveries during 1950, Simpson and Long proved the ill effects of delivery on active tuberculosis and they recognized a close connection between the stage of tuberculosis before delivery, and the rapid progress of the disease following it. They also shared the opinion that pregnancy should be interrupted in cases of active tuberculosis.

This opinion was radically changed by the modern treatment of pulmonary tuberculosis, i.e., the antimicrobial and surgical treatment. As a result of this treatment, the number of exacerbations following delivery dropped to such an extent that it did not exceed that prevalent in other cases of tuberculosis. There was a marked decrease in the number of indications to interrupt pregnancy for tuberculosis and today, if such measure is resorted to, it is mostly due to social reasons.

Material and Methods

This paper is based on the review of the clinical histories of 55 women who were delivered during the period 1952-57. They were hospitalized

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This article is based on our experience in the Malben Beer-Yaacov Hospital for Chest Diseases — Services of the American Joint Distribution Committee in Israel which receives its budget from the United Jewish Appeal.

at Beer Yaacov Hospital in a special ward where they were treated by a team of workers trained for attending such patients. The deliveries took place in the maternity ward of "Asaf Harofe" Hospital, which is located in the vicinity of our hospital. A few days after delivery, they were returned to us and treatment continued. In 31 (56 per cent) of the cases, the disease was discovered on routine x-ray film examination during pregnancy. Of these, 22 suffered from tuberculosis, 11 of them with cavitations. Of the rest, 24 cases were old tuberculosis patients, who suffered from the disease for many years, some of them with chronic active disease and most of them with inactive lesions. It is a firm belief in our country that hospitalization of pregnant tuberculous women for delivery purposes protects them from a relapse in tuberculosis and for this reason the chest clinicians used to hospitalize the great majority of such patients even with inactive disease.

The newborn babies were separated from their mothers immediately after delivery, and were given BCG and then transferred to proper institutions for the duration of their mothers' stay in the hospital.

The age of the patients ranged from 18 to 40. Thirty-five of them were admitted with active, and 20 had inactive lesions.

The distribution by stages of disease was as follows:

	ACTIVE			
		BK-positive with cavitation	BK-negative	INACTIVE
Minimal			1	
Moderately advanced	13	3	15	19
Far advanced	6	6		1
TOTAL	19		16	20

Of the 35 cases of active tuberculosis, 19 had cavitation (BK+). For 28 of the patients this was their first delivery, while for 27, their second or more. Those with active tuberculosis were immediately, upon the discovery of the disease, hospitalized in the fourth or fifth month of pregnancy. Those with inactive lesions were hospitalized in the eighth month of pregnancy, with the total length of hospitalization not exceeding four months.

During the years 1952-1955, all the patients received PAS and Nicotibin during pregnancy. In the last month of pregnancy and following delivery we also added streptomycin. Patients with severe tuberculosis received streptomycin also during pregnancy. From 1956 on, all with active tuberculosis received the three drugs immediately upon entring the hospital, and for the duration of their hospitalization. The antimicrobial treatment was given for six months up to two years, depending on the stage of the disease.

In one case, a segmentectomy was performed in the fourth month of pregnancy. In five of far advanced tuberculosis with cavitation of the lower lobes, we induced pneumoperitoneum after delivery and maintained it for a few months — in one of them, for about three years.

Results

The post-partum clinical course of the tuberculous process was observed in the hospital and after discharge from the chest clinics for periods ranging from five months to five years.

DURATION OF FOLLOW-UP OF THE PATIENTS AFTER DELIVERY

Time	Active	Inactive
Up to 6 month	12	9
Up to 12 months	9	5
1 — 2 years	7	1
3 — 5 years	8	4
TOTAL	36	19

Among the patients with inactive tuberculosis there was no case of exacerbation of the disease during the follow-up period. Among 35 patients suffering from active tuberculosis, 33 showed signs of improvement during pregnancy which persisted after delivery. Some of these women had far advanced cavitary tuberculosis which prior to the introduction of antituberculous drug treatment could not have reasonably been expected to go through with delivery without serious risk to life. Even these patients were delivered without difficulty and their post-partum clinical course was satisfactory.

In two cases only, there appeared an exacerbation of the disease during the first three months following delivery. Out of 19 patients suffering from tuberculosis with cavitation, 16 (84 per cent) became bacillus of Koch negative either during pregnancy, or after delivery; three remained bacteriologically positive. In not one case where a patient was negative during pregnancy did she become positive after delivery.

The following table illustrates the patients' state of disease at the end of the follow-up:

Case Reports

M. R., had far advanced bilateral pulmonary tuberculosis, with a giant cavity in the right lower lobe, bacillus of Koch strongly positive (Fig. 1). She was hospitalized in

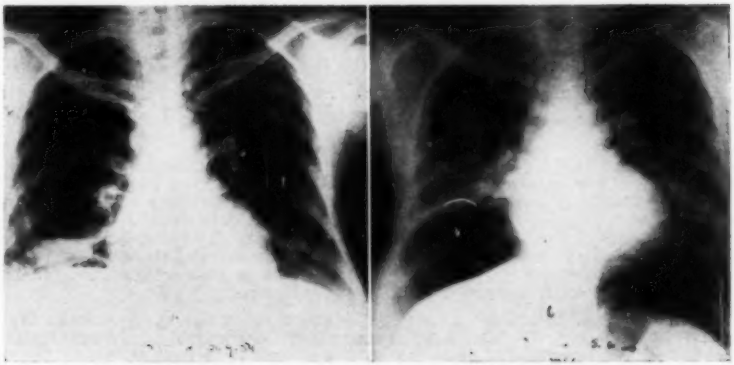


FIGURE 1 FIGURE 2

the seventh month of pregnancy in 1954. After receiving antimicrobial treatment, the cavity shrank considerably and marked absorption of the infiltrative changes was noted. After delivery, pneumoperitoneum was induced, the condition of the lungs improved gradually, and the cavity closed. She left the hospital well, bacillus of Koch negative (Fig. 2).

R. C., 21 years old, was hospitalized in December, 1954 because of exudative far advanced pulmonary tuberculosis, with a giant cavity in the right middle lung field (Fig. 3). In June, 1955, she became pregnant and was successfully delivered in March, 1956. After delivery pneumoperitoneum was induced. An x-ray film four months after delivery showed considerable improvement in the tuberculous process, i.e., disappearance of the giant cavity and absorption of the infiltrative changes (Fig. 4).

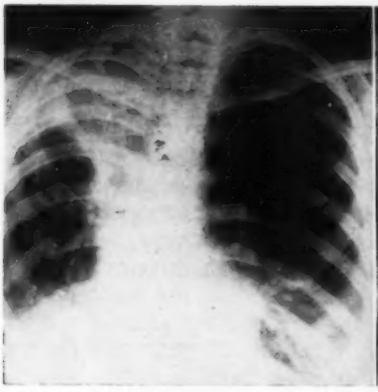


FIGURE 3

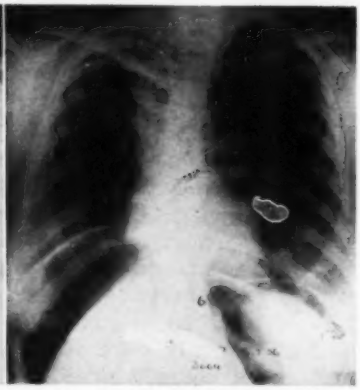


FIGURE 4

	ACTIVE			
		Koch bacillus positive with cavitation	BK-negative	INACTIVE
Minimal				1
Moderately advanced	1	1	2	48
Far advanced	2	2		1
	3		2	50

Discussion

After reviewing the material and checking the results of the treatment and the follow-up of patients after delivery, it seems to us that the fundamental problems to be answered are as follows:

a) Do pregnancy and delivery cause exacerbation of tuberculosis?

b) Should pregnancy be interrupted in cases of active tuberculosis?

c) What is the health condition of children delivered of mothers suffering from tuberculosis?

It seems from our findings that in the era of modern antimicrobial treatment, and especially long-term treatment, combined with moderate lung excisions, there is no reason to be afraid of exacerbation of the disease after delivery. The antimicrobial treatment, provided that full sensitivity to such drugs does exist, guarantees against exacerbation of the disease during and following delivery. The clinical course of active tuberculosis during pregnancy and after delivery is not substantially different from that in non-pregnant women and the lesions respond to antimicrobial treatment during pregnancy and after delivery in a satisfactory manner.

The antimicrobial treatment also permits excisions in the early months of pregnancy without untoward effects on the pregnancy. According to our experience, the percentage of exacerbation is quite low and it is similar to that shown in the report of Schaefer, which is based on a follow-up of 255 women. Pregnancy and delivery have no effect whatsoever on inactive tuberculosis. According to our material, as well as

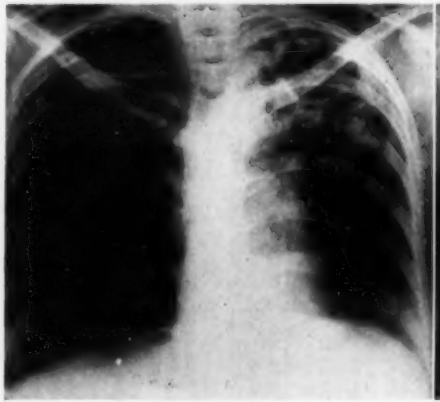
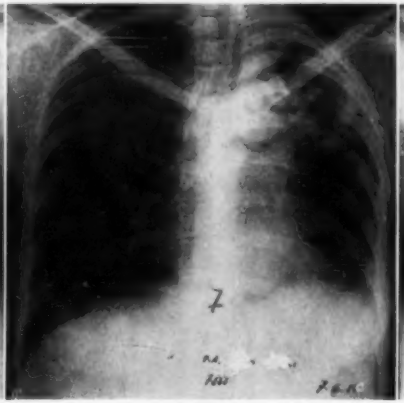


FIGURE 5



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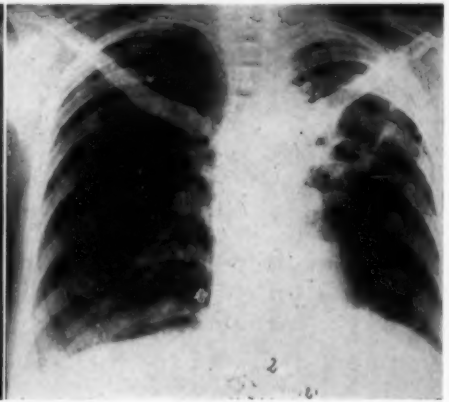

FIGURE 7

J. R., 32 years old, who had suffered for many years from far advanced, pulmonary tuberculosis on the left side with cavitation, became pregnant in 1955. She entered our hospital in May, 1955 (Fig. 5) to be delivered. X-ray films taken five months after delivery did not show any deterioration in the patient's condition (Fig. 6). In spite of our repeated warnings, she became pregnant again, and delivered in February, 1957. She was hospitalized again and x-ray films taken five months after delivery did not show exacerbation of the disease (Fig. 7). She has been consistently Koch bacillus positive. It is worth noting that in spite of prolonged treatment, no drug resistance developed and this is probably the reason why anti-tuberculosis drug treatment given during pregnancy and after delivery protected her from relapses.

that of Schaefer, no patient was found who deteriorated following delivery. In view of this, the question may be raised: Is it still advisable to interrupt pregnancy, for medical reasons, in pulmonary tuberculosis?

Various medical people point to the possibility of exacerbation of the disease as a result of an abortion. In our experience, which is based only on a small number of tuberculosis patients who underwent abortions for social reasons, we also observed definite deterioration in the condition of a woman whose pregnancy had been interrupted.

H. S., 28 years old, was hospitalized because of infiltrative, bilateral, process with cavitation. Following antimicrobial treatment the cavities closed. During the period of hospitalization the patient became pregnant and, due to social reasons, an abortion was done. About a month later, one of the cavities re-opened. It would seem to us that in this case the deterioration in the patient's condition may have been caused by the abortion.

We should not forget that interruption of pregnancy endangers the life of the patient, and may be the cause of future sterility. According to Klintskog, the mortality is 0.6 per cent, and sterility 2.7 per cent. Considering this, and also the fact that the percentage of exacerbation of the disease during pregnancy and delivery is very small, it is our opinion that in the era of modern treatment of tuberculosis there is no justification for surgical interruption of pregnancy in patients suffering from this disease.

Now, as to the health condition of the newborn. It is well known that hereditary tuberculosis is rare. All the patients selected for our survey had given birth to healthy children, free from tuberculosis. The infants received BCG immediately after delivery. As the BCG takes effect only after 6 to 8 weeks, it was necessary to separate the infants from their mothers during this period, and to place them in suitable institutions. Not one infant contracted tuberculosis. The antimicrobial drugs, including streptomycin, given the patients during pregnancy, had no ill effects on the infants, and had caused no complications.

CONCLUSIONS

1. Active pulmonary tuberculosis does not present a reason for interruption of pregnancy.
2. Delivery has no influence on the tuberculous process.
3. Routine fluoroscopy during pregnancy is an effective means for discovering pulmonary tuberculosis.
4. Infants born to mothers suffering from tuberculosis are free from the disease and have regular average weight.
5. Antimicrobial drugs given to tuberculous patients during pregnancy have no ill effects on the newborn and do not cause complications.
6. Close cooperation between the lung specialist and the obstetrician is essential to the treatment of a pregnant woman suffering from tuberculosis.

SUMMARY

This is a report on a follow-up of 55 cases of pregnancy in women with pulmonary tuberculosis who were hospitalized at the Malben Hospital in Beer Yaacov during the years 1952-1957. All received antimicrobial treatment during pregnancy and also after delivery. Only two active cases showed signs of deterioration after delivery. In all other cases there was no change in the tuberculous process after delivery, unless for the better.

In a follow-up of patients subsequent to delivery, no case of exacerbation of the disease was noted and we found no complication in the condition of the mothers or the infants as a result of having received antimicrobial treatment. It is possible to perform lung excisions and other chest operations during pregnancy, without untoward effects.

RESUMEN

Esta es una relación de la observación de 55 casos de mujeres tuberculosas embarazadas ingresadas al Hospital Malben en Beer Yaacov, durante los años de 1952-1957.

Todas recibieron tratamiento antimicrobiano durante el embarazo y después del parto. Sólo dos casos activos mostraron empeoramiento después del parto. En todos los demás no hubo cambio en el padecimiento tuberculoso después del parto y si lo hubo, fué hacia la mejoría.

La observación de los enfermos después del parto, dejó ver que no hubo ningún caso de exacerbación de la enfermedad y no encontramos complicación en las madres o en los niños por haber recibido tratamiento antimicrobiano. Es posible realizar resecciones pulmonares y otras operaciones durante el embarazo sin malos resultados.

RESUMÉ

L'auteur rapporte l'observation complète de 55 cas de grossesse chez des femmes atteintes de tuberculose pulmonaire hospitalisées à l'Hôpital Malben de Beer Yaacov pendant les années 1952 à 1957. Toutes reçurent un traitement antibacillaire pendant la grossesse ainsi qu'après l'accouchement. Deux cas seulement montrèrent des signes d'aggravation après l'accouchement. Dans tous les autres, il n'y eut aucune modification du processus tuberculeux après l'accouchement, si ce n'est une amélioration.

Dans un examen systématique des malades après accouchement, on ne nota aucun cas d'exacerbation de la maladie, et on ne trouva aucune complication dans l'état de santé des mères ou des bébés, provenant de l'administration d'un traitement antibacillaire. Il est possible de pratiquer des exérèses pulmonaires et autres opérations thorariques pendant la grossesse sans effet nocif.

ZUSAMMENFASSUNG

Bericht über eine Nachuntersuchung von 55 Fällen von Schwangerschaft bei Frauen mit Lungentuberkulose, die in den Jahren 1952 - 1957 im Malben-Krankenhaus in Beer Yaacov stationär behandelt wurden. Sie alle hatten eine antimikrobielle Behandlung bekommen während der Schwangerschaft und nach der Entbindung. Nur zweiaktive Fälle zeigten Symptome einer Verschlechterung nach der Entbindung. Bei allen anderen Fällen gab es keine Veränderung des tuberkulösen Prozesses nach der Entbindung, es sie denn im günstigen Sinne.

Bei der Nachuntersuchung von Patienten im Anschluss an die Entbindung wurden keine Fäll Exacerbation der Erkrankung ermittelt, und wir fanden keine Komplikationen im Zustand der Mutter oder des Säuglings als Folge dessen, dass eine antimikrobielle Behandlung vonstatten gegangen war. Es ist möglich, Lungenresektionen und andere Thoraxoperationen während der Schwangerschaft auszuführen-ohne ungünstige Auswirkungen.

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A Timed Vital Capacity Recording Device

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Glenn Dale, Maryland

Since Gaensler's article[1] appeared in 1951, the value of the "Timed Vital Capacity" test has been eminently confirmed. With one test, the presence of both restrictive and obstructive ventilating defects is demonstrated. Here presented is a device that has been used for four years as the first step in the evaluation of lung function of all candidates considered for pulmonary surgery at the Glenn Dale Hospital.

It is a very rapid method. The results are recorded graphically, several tracings being made at one sitting. No calculations need be made since a nomogram is used. There has been no mechanical failure or has the unit required recalibration. Ten patients may be examined, evaluated and reports completed in one hour.

Materials and Methods

This apparatus operates as a floating pen moved vertically by a spirometer. A cam produces lateral pulses or "pips" at one second intervals

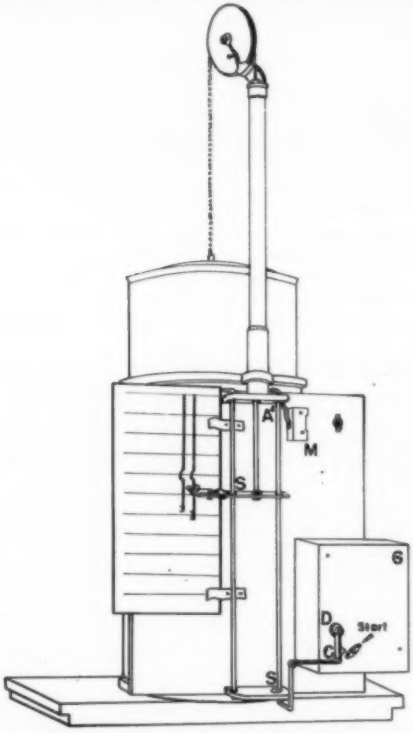

FIGURE 1: A timed vital capacity recording device. The microswitch, motor and line switch wired in series. Two vital capacity tracings are shown.

*From Thoracic Surgical Service, Glenn Dale Hospital and the Department of Public Health of the District of Columbia.

along the vertical line. The pen carriage moves on (A) as the axis — the 2 slots (S) permitting lateral motion. (Fig. 1) A 10″ x 14″ masonite board is mounted by cleats to the back of a Collins "Vitalometer." The cleats support the two track rods, one of which hangs loosely at A. A 30 rpm. motor is mounted as shown.

The cylindrical counter balancing weight is tapped to accept a short ¼ rod to which the pen carriage rod is attached by rubber tubing. In spite of the weight of the pen carriage, it was found necessary to add 10 grams in addition so that the unit was evenly balanced at the end of a tracing.

A standard laboratory ink cup is mounted near the end of the carriage so that it may be rotated for positioning and cleaning.

Hinge (C) floats — being fixed at a pivot point (D) and attached to the movable rod. "Start" is the point to which the cam is directed at the start of a run. This point must be located with a stop watch or other suitable device so that from the time the microswitch (M) is released and the first second indicated by the pen — exactly one second has elapsed. Recording paper is constructed so that the transverse lines represent intervals of 0.5 liters. The vital capacity in liters then is read directly as the length of the tracing.

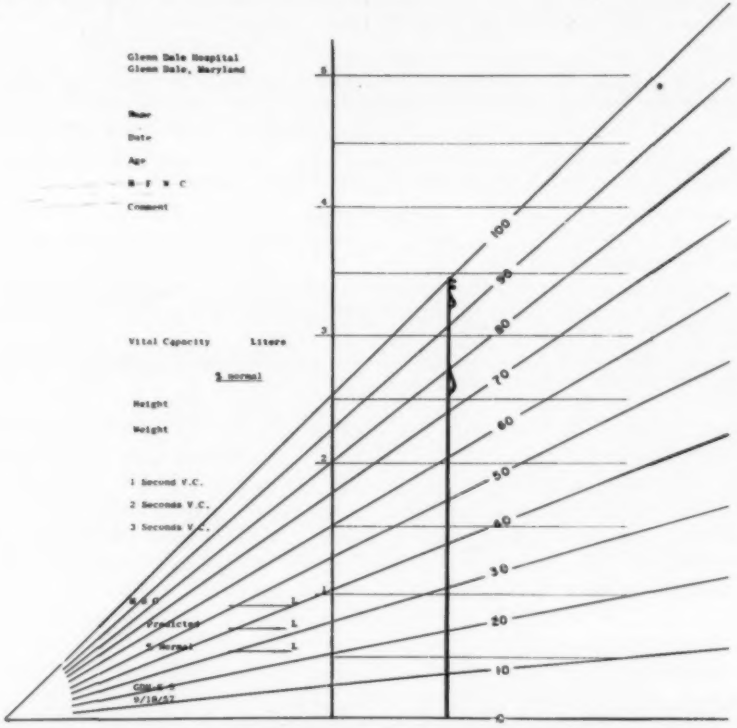

FIGURE 2: Analysis of a single tracing. A transparent grid has been placed over the recording paper. The vital capacity is 3.4 liters. First second, 75 per cent; second second, 94 per cent; third second, 98 per cent.

The Recording paper is folded and inserted upside down. The pen is raised to its maximum height. This opens the microswitch. As soon as a patient expires into the apparatus, the motor* immediately starts. At the end of expiration there will be no further motion of the pen downward and pips become superimposed on each other. At this point the operator turns the switch off, the cam directed to the starting point again and the pen carriage is elevated for the next tracing.

Mounting clips for the paper are made long enough so that the paper may be withdrawn a few millimeters between each tracing.

The percentage of normal vital capacity is obtained by Meyer's tables or Baldwin, Cournand and Richards.[2]

The speed of expiration is obtained by placing a transparent grid over the most suitable tracing (Fig. 2) so that the extent of the vital capacity lies exactly between 0 and 100. The first, second, and third second pips are then apparent as percentage of the total vital capacity and so recorded.

SUMMARY

An instrument is presented which records multiple Timed Vital Capacity measurements in a form that may be readily interpreted.

RESUMEN

Se presenta un aparato que registra múltiples medidas de la capacidad vital en relación al tiempo, en una forma fácil de leerse.

RESUMÉ

L'auteur présente un instrument qui enregistre les multiples mesures de capacité vitale sous une forme qui permet leur interprétation rapide.

ZUSAMMENFASSUNG

Beschreibung eines Instrumentes, das mehrfache Vitalkapazitätsbestimmungen in einer Form aufzeichnet, die ihre alsbaldige Auswertung ermöglicht.

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*The motor used is a "Gear Motor" made by the Motoresearch Company of Racine, Wisconsin. Thirty revolutions per minute.

The Use of Premarin IV in Hemoptysis

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Following the reading of a report by Menger[1] on "Estrogen given Parenterally to Control Epistaxis and Hemorrhage after Adenoidectomy," a search of the literature failed to reveal a report on the use of estrogen for a form of bleeding which is fairly commonly associated with more or less advanced cases of pulmonary tuberculosis. Previous to Menger, Jacobson[2,3] reported on the use of Premarin IV in "Spontaneous Hemorrhage" associated particularly with epistaxis and waxed so enthusiastic about the results as to advance the theory that "Spontaneous Hemorrhage" was a clinical entity. Others have since reported on the use of Premarin IV in ocular bleeding, in dentistry, in gastro-intestinal and genito-urinary hemorrhage, all with glowing results. This, then, is a report on the use of Premarin in the control of severe hemoptysis complicating pulmonary tuberculosis.

At the Rush Hospital, devoted mainly to diseases of the chest it frequently became necessary to deal with the problem of hemoptysis. Until the advent of Premarin IV, the usual routine employed in the management of a case varied with the severity encountered. In mild cases exhibited by the expectoration of small amounts of pure blood or blood-stained mucus, rest and sedation were sufficient. In a day or two, this regimen sufficed to stop the bleeding. However, in severe cases with expectoration of 120 cc. or more of pure blood more strenuous measures were employed; thus were added ice-bag to chest, drugs such as adrenosem, ascorbic acid and synkavite. Occasionally, when the above measures did not suffice, pneumothorax or pneumoperitoneum and sometimes transfusion were employed. The subsidence of hemorrhage was awaited with apprehension by patients and attendants alike. Several days were required for bleeding to cease.

Stimulated by the appearance of Menger's paper in 1955, the use of Premarin was tried for the past three years in severe cases of hemoptysis. During this time 14 cases have been collected. To give this drug a fair trial it was decided to limit its use to patients expectorating at least four ounces of pure blood; in other words, to patients whose bleeding gave us concern. The result was immediately apparent; bleeding stopped within minutes. Indeed, in our early cases it was considered as mere co-incidence that bleeding was immediately controlled, but as this experience repeated itself, we were convinced no previous drug or measure had had this effect. In nine of these patients, bleeding was controlled after a single injection of Premarin. In four, a second injection was necessary in 24 hours on account of recurrence of bleeding. In one patient, three injections were required nine hours apart.

It is idle to speculate on the kind of tuberculous infection that may be expected to bleed. In our experience, cases have no recognizable pattern of pulmonary hemorrhage. Here, as in any other human endeavor, individual variations occur; thus death followed in one patient from

Acknowledgment is made of the contribution of Premarin IV by the Ayerst Laboratories, New York.

exsanguinating hemorrhage three weeks after Premarin IV was sucessfully employed for excessive bleeding. In this case, however, the patient was found dead in a pool of blood before any therapy had been administered. Much too, depends on the kind of pathology present; thus, in a personal communication, bleeding from carcinoma of the lung was not affected by the administration of Premarin. Another individual variation occurs in the length of time Premarin IV is effective. In our limited experience, this is from nine hours on, depending on the effective treatment of the disease. Thus far our cases have one thing in common and that is the response to the administration of Premarin IV.

Method of administration: Following directions accompanying the package, 5 cc. of diluent is extracted from a vial with a 5 or 10 cc. syringe and added to a rubber-stoppered bottle containing 20 mg. of powdered Premarin. Solution is prompt without shaking. The resulting clear amber solution is then injected intravenously consuming about 20 seconds for this procedure.

Action: The mode of action of Premarin IV is still undetermined. Of one clinical fact we are certain and that is that the effect is practically immediate. Johnson[4] working with dogs concluded so far that Premarin caused an increase in the coagulability of blood. Clinical corroboration of this finding in the human is the occurrence of small clots of blood in the sputum of patients who have received Premarin. This finding persists for a few days, the sputum subsequently remaining clear. Mention should here be made of the fact that no reaction of any kind has been so far encountered, and that is also true of thrombi in any part of the body.

SUMMARY

In an experience with 14 cases of severe hemoptysis complicating pulmonary tuberculosis, the administration of Premarin IV was strikingly effective in the control of hemorrhage. It appears therefore that in Premarin IV we have a valuable addition to our armamentarium in the management of this emergency.

RESUMEN

En una experiencia con 14 casos de hemoptisis grave complicando a la tuberculosis la administración de Premarin IV fué notablemente efectiva para el control de la hemorragia. Parece por tanto que con ese medicamento, contamos con una valiosa adición para el tratamiento de esa emergencia.

RESUMÉ

Dans une étude de 14 cas d'hémoptysies graves compliquant une tuberculose pulmonaire, l'administration de "premarin IV" fut nettement efficace et permit l'arrêt de l'hémorragie. C'est pourquoi il semble que nous ayions dans la "premarin IV" un supplément valable à notre armement pour le traitement de cette urgence.

ZUSAMMENFASSUNG

Bei einem Experiement an 14 Fällen mit schwerer Blutung als Komplikation einer Lungentuberkulose erwies sich die Anwendung von Premarin IV als von einwandfreier Wirksamkeit bei der Bekämpfung der Blutung. Es scheint daher, daβ wir im Premarin IV eine wertvolle Bereicherung im Rüstzeug zur Behandlung dieses Notstandes haben.

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SECTION ON CARDIOVASCULAR DISEASES

The Complete Relief of Mitral Stenosis: Ten Years of Progress Toward This Goal

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PART II

(Conclusion)

Part I of this article appeared in the May issue of this Journal. It contained a discussion of the factors which led to the modern surgical procedure for the relief of mitral stenosis as well as a description of the technique involved. The surgical concept underlying the old technique is based on a limited understanding of the condition. Mitral commissurotomy (left-sided technique) neither aims at nor accomplishes complete relief of the stenosis. Persistent efforts in an attempt to improve the operation throughout the last decade have resulted in a new surgical concept which involves the creation of a functional valve of a different type. The anatomical and pathological factors underlying this operation were described as well.

Results of the New Operation

Although the "right sided approach" to the mitral valve has been utilized by us since 1954,[17] the technique used for the actual relief of the obstruction of the valve, even when performed from the right side was based at the beginning mostly upon the concept of division of the tissue occupying the commissural scar lines, i.e. commissurotomy. Only since September 1955 has the technique of fashioning of a new septal leaflet (hinging) been applied by us consistently. From that date until July 1, 1958, a total of 462 patients with pure or preponderant mitral stenosis have been operated by us. This constitutes the total patient population presenting itself at our clinic during this period for the relief of mitral stenosis.

The extent to which the stenotic valve was surgically enlarged and functionally reconstituted by the new technique in 460 patients (2 patients died prior to actual cardiotomy) is shown in Table 3.

As will be noticed the estimates of surgical accomplishment are expressed in percentage of normal valve function. It is unfortunate that no truly objective criteria for valve size and function are available and that one must rely upon the admittedly rough approximation of the accomplishment which the surgeon can proffer. Attempts at expressing the opening achieved in quasi-objective terms of square centimeters,

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The research work basic to the development of this method of treatment was supported by the Mary Bailey Institute for Heart Research, Philadelphia, Pa.

as measured by the size of the intracardiac finger and its freedom of movement within the valve orifice, even when repeatedly compared with standard openings of known area are notoriously unsatisfactory. The intracardiac finger may with ease separate the edges of the divided valve after commissurotomy to an extent which the pressure within the left atrium, even when markedly increased can never duplicate. With the "hinging" method, on the other hand, the newly fashioned "septal leaflet" properly freed subvalvularly, will move effortlessly downward and forward into the ventricle producing such a wide opening that measurement of the diastolic aperture in terms of finger size becomes impractical.

The accuracy of estimation of post-operative valve opening and function as described by the surgeon in percentage of normal in this series is best judged in the light of Table 4. This table reveals that the apical middiastolic murmur (probably the most sensitive indicator of obstruction at the mitral valve) disappeared in 55 per cent of those patients who received a good functional opening (estimated at 80-100 per cent of normal) by this method.

The factors which militated against the achievement of a 100 per cent functional opening in every case in this series are many. The presence of calcification of the valve as well as the severity of other pathological changes influenced the surgical accomplishment to some extent. Of considerably more importance, however, is the way in which the patient reacts to the manipulations. Severe hypotension following manipulations at the valve, particularly when the blood pressure fails to return to normal values promptly, indicates an extremely precarious condition of the patient. Under such circumstances the surgeon will, more often than not, desist from completing the desirable degree of mobilization of the valve and accept a compromise result.

Incompetence of the valve plays a primary role in limiting the extent of the surgical accomplishment. In cases with pre-existing insufficiency of more than negligible degree the surgeon may hesitate to separate the valve in the vicinity of the incompetent commissure for fear of increasing the amount of regurgitation. For the same reason, even the most minimal degree of valvular insufficiency created surgically is taken as an indication for desisting from further mobilization in the vicinity of the regurgitant jet. Table 5 demonstrates the degree of valve competence before and after the operation. The quantitative description of the insufficiency is based upon the surgeon's evaluation of the intra-atrial jet felt during ventricular systole. The high incidence of minimal incompetence is an inherent consequence of the philosophy of methodically carrying the valve cleavage to the point of first recognition of a minimal (physiologically insignificant) regurgitant jet.

TABLE 3—ESTIMATION OF PERCENTAGE OF RESTORATION OF FUNCTION AFTER "CREATION OF A SEPTAL LEAFLET" 460 Cases (1955-1958)

80% - 100% function	70 per cent
Less than 80% function	30 per cent
Due to fear of aggravating insufficiency	7 per cent
Compromise result for other reasons	23 per cent

TABLE 4—DISAPPEARANCE OF DIASTOLIC MURMUR AFTER "CREATION OF A SEPTAL LEAFLET" IN 423 PATIENTS IN WHOM PRE- AND POST-OPERATIVE CARDIO-PHONOGRAPHIC RECORDINGS WERE MADE

Extent of Functional Restoration	Patients Operated	Disappearance of Diastolic Murmur	Percentage
		No. of Patients	
80% - 100%	304	167	55
Less than 80%	119	37	31
Total	423	204	48

The incidence of thrombosis of the atrial appendage and upon the atrial wall proper as recognized at operation is presented in Table 6. The higher incidence of thrombosis of the left atrium in the report of the American College of Chest Physicians and in our older series as compared to the incidence in the latest series (462 patients) is probably explained by the fact that the surgeon approaching the valve through the appendage (left-sided approach) necessarily will notice practically every thrombus present while the one using the right-sided approach will not feel obliged to take great pains to detect thrombi situated deeply within the appendageal tip.

Only 9 of the 48 thrombi found in this series of 462 patients were deemed to require removal. This was accomplished by passing a suitable Litwak suction tip into the left atrium[20] through the right sided cardiotomy wound along the palmar aspect of the surgeon's finger.

The incidence of operatively created arterial embolization in this series was only 2.8 per cent. Two patients with cerebral embolization

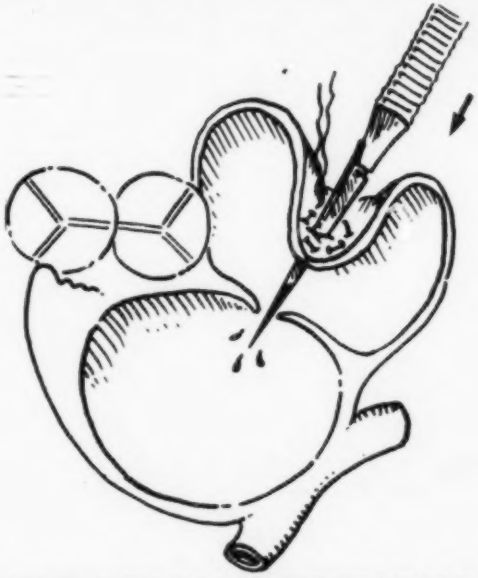

FIGURE 15: Emergency creation of a small atrial septal defect to relieve acute pulmonary edema especially when caused by the inability of the left ventricle suddenly to accept the increased transmitral blood flow after relief of mitral stenosis. Such defects, unless very large, close off within a few weeks. Bailey *et al*, Courtesy of *Advances in Cardiology*, Editor: Prof. R. Hegglin. (S. Karger Ltd. Basle, Switzerland, 1959).

died, resulting in a 0.4 per cent mortality rate from embolization in this series.

The over-all operative mortality for the 462 cases was 5.8 per cent. The causes of death are detailed in Table 7.

A follow-up study of 107 patients who had a good technical result (80-100 per cent functional opening) following the new operation is presented in Table 8. The evaluation of their condition is based upon the patient's self appraisal in addtion to whatever objective data could be obtained from their physicians or by re-examination by one of our cardiological associates.

Evaluation of the New Operation

In contradistinction to the old commissurotomy procedure, the new operation which creates a freely hinging "septal leaflet" should be and can be evaluated by objective criteria. To the extent to which the fashioning of a new and grossly competent valve mechanism is achieved surgically (in line with our more complete understanding of the normal as well as the pathological mitral valve) the results are eminently gratifying.

The apical mid-diastolic murmur in mitral stenosis is probably the most sensitive of all the objective signs indicative of obstruction at the valve level. The mildest degree of stenosis of the mitral valve even though completely asymptomatic and probably without any physiological significance usually can be diagnosed with confidence by recognition of the typical diastolic murmur. Cardiac catheterization of the left side of the heart under these circumstances would probably reveal completely normal physiological data. It is conceivable that with severe physical exertion which approaches the limit of cardiac functional reserve, a gradient across the mitral valve might develop in these patients but this, at least with the methods at our disposal, would be difficult to demonstrate.

We are probably entitled to believe that the complete abolition of the diastolic murmur is indicative of practically complete correction of the stenosis. The abolition of the diastolic murmur in 55 per cent of the patients in whom a satisfactory neostrophingic mobilization was carried out (70 per cent of the series) in comparison with the 8 per cent obliteration following the older operation clearly indicates, therefore, the superiority of the newer procedure.

In the light of such objective signs of abolition of the obstruction at the valve the subjective appraisal of the patient with respect to symptomatic improvement would seem less significant. A comparison of

TABLE 5—REGURGITATION AT THE MITRAL VALVE (SURGEON'S OPINION) BEFORE AND AFTER "CREATION OF A SEPTAL LEAFLET" (460 Patients)

Amount of Regurgitation	Preoperative		Postoperative	
	No. of Patients	Per Cent	No. of Patients	Per Cent
None	345	75	105	23
Minimal (Insignificant)	106	23	324	70
Moderate (probably significant)	9	2	25	5½
Severe			6**	1½

**All Fatal

follow-up figures with respect to subjective improvement after commissurotomy, and the new operation on the other hand, may not show any impressive gain for the newer procedure. This evaluation is misleading in two respects. First, the "self-appraisal" of the patient is actually to a considerable degree an interaction of patient and physician appraisal in which the physician probably plays the major role. A physician who considers surgical treatment for mitral stenosis, whatever the technique, as basically but a palliative procedure (undoubtedly the prevalent opinion)[11,14] usually will not permit the post-operative patient to test his functional capacity to the limit even while apparently encouraging him to retrun to a "normal life" and full employment. When, on the other hand, we shall succeed, as we hope, in convincing our medical colleagues everywhere that the obstruction at the mitral valve can be removed completely and the valve returned to full or nearly full function, the situation may be completely different. We are looking forward to the time when, allowing for a convalescent period to permit the more gradual disappearance of secondary physiological changes such as pulmonary hypertension (unless, of course, of extreme degree), many patients will be urged to return to a completely normal life with unrestricted physical activity.

Secondly, the "self-appraisal" of any patient necessarily is elicited at a given cross-section of time. Thus the picture is presented in static form only. Seen dynamically, however, we know that the maximal subjective improvement after commissurotomy is obtained within a few months following the operation. It has been documented repeatedly that there is a progressive falling off in the percentage of "good" results with the passage of time.[1,11,15] In many cases this portends the appear-

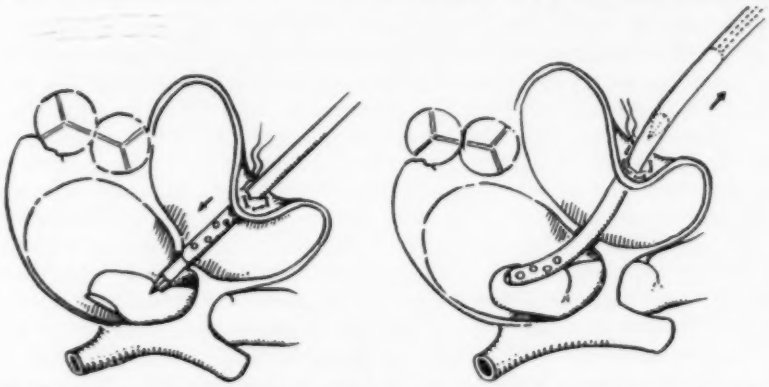

FIGURE 16: Simple method for simultaneous creation of a small "balancing" atrial septal defect and cannulation of the left atrium.

FIGURE 16-A: A multi-windowed plastic catheter is "stiffened" by insertion of a Fitch pointed obturator. With the tip of the operator's left index finger within the left atrial chamber (having entered by the usual dissection of the interatrial groove) for control, the obturator and catheter are caused to pierce both a purse-stringed area of the right atrial wall and the thicker dorsal portion of the atrial septum.

FIGURE 16-B: Removal of the obturator leaves the fenestrated portion of the catheter within the left atrial chamber. Upon termination of the perfusion removal of the catheter will establish a small and transitory but functional atrial septal defect which can decompress the left atrium adequately. Bailey et al, Courtesy of *Advances in Cardiology*, Editor: Prof. R. Hegglin. (S. Karger Ltd. Basle, Switzerland, 1959).

ance of the spectre of restenosis. In the case of the newer operation, since the valve cleavage is extended well into flexible and grossly uninvolved tissue the resulting functional restoration may be expected to be permanent. Restenosis would seem to be precluded in the absence of a recrudescence of rheumatic activity. Symptomatic improvement not only may be expected to be maintained but should become enhanced by the progressive disappearance of secondary physiological disturbances with the passage of time. Our more optimistic prognosis for the patient who has had the new procedure, although based upon seemingly sound theoretical considerations, must, of course, still await the test of time.

Some improvements in the results of this operation when compared with mitral commissurotomy are due, not to the new concept of repair of the valve but to the "right-sided approach," per se. This pertains especially to the safety of the surgical manipulations in terms of atrial tears and dislodgement of thrombotic material. Except for our early developmental experience with the right-sided approach when there were two instances of fatal hemorrhage from the atrium, this technique has proven eminently safe. The technical safeguards which have been published[11] apparently have abolished the danger of atrial hemorrhage so that in our last 300 cases there has not been a single instance of major hemorrhage from the atrium.

The improvement with respect to reduction in the incidence of arterial embolization, especially that resulting in the death of the patient is also quite impressive. Since the site of surgical entrance into the heart is far removed from the area in which thrombi are most commonly found, in contradistinction to that of the trans-appendageal entrance (left-sided approach) this improvement presumably can be credited to the right-sided approach itself.

The creation of mitral incompetence is an inherent risk of any type of surgical procedure for the relief of mitral stenosis. Table 5 shows that the incidence of recognition of a new regurgitant jet during the new procedure is reported to be somewhat higher than with the older commissurotomy technique. There can be no doubt that the creation of physiologically significant regurgitation would be too high a price to pay for the relief of the stenosis. On the other hand, there are undoubtedly degrees of minimal incompetence (as measured by the jet felt in the left atrium) which are of no functional significance. In between the completely insignificant and the physiologically definitely significant degrees of regurgitation it may sometimes be extremely difficult for the surgeon to evaluate the regurgitant jet categorically. However, since the earliest appearance of a minimal regurgitant jet serves as an indica-

TABLE 6—INCIDENCE OF THROMBOSIS IN THE LEFT ATRIUM

	Thrombi Found	
	No. of Patients	Per Cent
American College of Chest Physicians (938 Patients)	207	21.0
Bailey Clinic (811 Patients—Left-sided approach prior to 1955)	242	29.9
Bailey Clinic (462 Patients—Right-sided approach)	48	10.5
Removed at operation	9	
Left undisturbed	39	

tion for desisting from further mobilization of the valve (in that area) the great majority of jets defined as minor in Table 5 were those which we consider to be completely insignificant. The fact that force is not applied to the valve structures indiscriminately, but rather in moderation and with deliberation in relation to easily recognized anatomical and pathological points of reference, suggests that the danger of creating degrees of marked or even severe incompetence with this technique is relatively small. Most instances in which major degrees of mitral insufficiency were produced were those in which, due to deterioration in the condition of the patient, the surgeon felt obliged to achieve an effective opening as quickly as possible and could not proceed with the desired degree of deliberation. Under such circumstances, of course, any technique carries profound additional risks. Our desire to prevent the development of situations which force the surgeon to act hastily and without due care has been instrumental in evolving a new technique of circulatory support which will be discussed later.

Although the surgeon's evaluation of the regurgitant jet probably provides the most accurate estimation of the degree of incompetence available at present, a project is at this time in progress at our clinic which will attempt to relate this to clinical terms of reference. This project in terms of ventriculographic studies and follow-up in cases with operatively produced regurgitant jets will, we feel sure, support our impression of the benignity of a "minimal degree of regurgitation" in the great majority of instances.

While the "right-sided approach" combined with the new concept for valve reconstitution (neostrophingic mobilization) has clearly, and in objective terms, proven its superiority over earlier techniques, our experience with our present series has been disappointing in two important respects. As can be seen from Table 3, in practice we did not achieve a fully satisfactory valve opening, in 30 per cent of the cases, and as

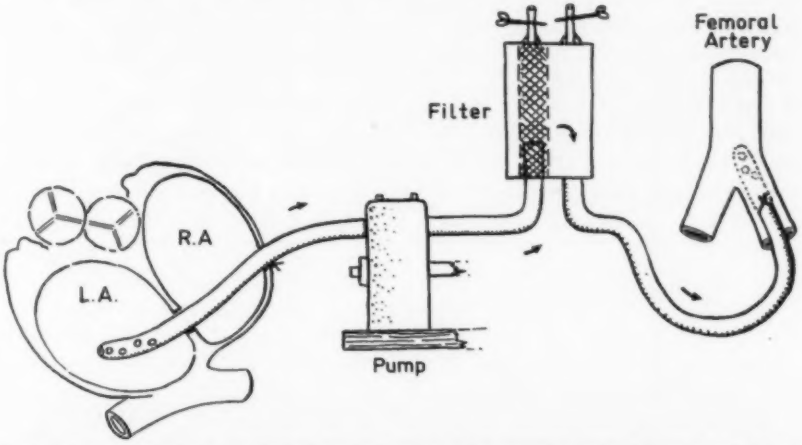

FIGURE 17: Diagram of closed bypass system for routine subtotal support of left ventricular function during surgical correction of mitral stenosis. The priming of this system requires but a minimal quantity (300 cc) of citrated blood. Bailey et al, Courtesy of *Advances in Cardiology*, Editor: Prof. R. Hegglin. (S. Karger Ltd. Basle, Switzerland, 1959).

shown in Table 7 the over-all operative mortality has not been reduced as drastically by this technique as we had hoped.

The vague realization that some basic weakness has existed in the surgical management of mitral stenosis even with all the technical improvements described has been with us for some time. The final crystalization of ideas resulting from the analysis of the results of this series has recently lead to a fundamental conceptual and technical augmentation of our armamentarium.

"Physiological" versus "Anatomical" Approach

While surgery is a discipline which is concerned primarily with the creation of anatomical changes for therapeutic purposes, the most significant advances of modern surgery have come about as a result of understanding and control of physiological aspects which are related to the anatomical changes. This involves among other things the maintenance of essential functions during the actual anatomical correction and the prevention of untoward physiological changes which may result from the surgical interference. Although the surgical treatment of mitral stenosis as we know it today is a creation of the last decade during which time physiology has gained its present preeminence in the whole field of surgery, surgeons dealing with the correction of mitral stenosis have concentrated mainly upon the anatomical changes to be produced at the operating table. This does not mean, of course, that extensive pre and post-operative physiologic studies of the circulation have not been carried out in many clinics. However, while this information has been useful in the understanding of the disease, it has not yet been incorporated actively into the surgical techniques.

When one considers that the left ventricle is an organ the effective function of which is an absolute prerequisite for moment-to-moment survival of the organism, it is nothing short of surprising that surgeons (and we too, must profess our guilt in this respect) have not hesitated to interfere grossly with its essential function during surgical manipulation of the mitral valve. Secondly, while during the past generation there has been a general realization that the sudden reversion of pathological structures to anatomical normalcy or near normalcy may produce acute physiological dysfunction to which the organism may not be able to accommodate immediately, the prevention of such

TABLE 7—CAUSES OF OPERATIVE MORTALITY
"CREATION OF A SEPTAL LEAFLET" (462 Cases)

		Total
Acute Heart Failure		
Arrest, Fibrillation, Hypotension	6	
Pulmonary Edema	7	13
Died Before Valve Reached		2
Major Regurgitation Created		6
Other Causes		
Cerebral Embolism	2	
Septicemia, Staphylococcal	2	6
Hemorrhage from Atrial Incision	2	
		27=5.8 per cent

sudden changes has not been given due consideration in the surgical treatment of mitral stenosis. Careful evaluation of the less satisfactory aspects of the new (or any) operation for mitral stenosis, has convinced us that the production of such sudden physiological changes are responsible for a considerable number of compromise results as well as for the still too high mortality rate. As an illustration let us discuss Table 8 which describes the causes of the operative mortality in the reported 462 cases.

The two cases of fatal infection from resistant staphylococci are an expression of the residual infectional hazards of cardiovascular surgery in the present era of comparative safety from serious infection. This type of fatality, however, is in no way related specifically to operations for mitral stenosis, and its discussion, therefore, will not add particularly to this evaluation.

The two cases of fatal hemorrhage during operation were the results of our early lack of experience with the "right-sided approach" and as stated previously can, with present knowledge and specific safeguards, be prevented in the future.

The two cases of fatal cerebral arterial embolization express a specific hazard of any surgical procedure performed within the chambers of the left side of the heart. Although considerably reduced with the "right-sided approach" (there has not been a single case of fatality from this cause in the last 250 consecutive cases) it is improbable that this complication ever will disappear completely.

Probably all of the remaining 21 deaths can be related to one of the specific physiological considerations mentioned above. All of the patients died as the immediate result of the operation either on the operating table or as a direct continuous effect from it. Two patients died, in fact, even before the definitive part of the operation could be carried out. In six cases major mitral insufficiency, created during desperate maneuvers in patients requiring immediate relief of the obstruction because of their precarious condition on the operating table, was the price paid for a hasty and indeliberate manipulation. In the remaining 13 cases, acute circulatory failure in one form or another, acute pulmonary edema, arterial hypotension, or cardiac arrest was the result of the physiologic insult to the circulation either during or following the manipulations. We are unable to document completely the considerably larger group of patients who manifested similar evidences of circulatory failure but who recovered in the end.

What are the immediate untoward physiological developments which may result from an operation for mitral stenosis? Basically they are two:

1. The left ventricle even when most carefully handled during the course of an operation on the mitral valve necessarily must suffer in two

TABLE 8—FOLLOWUP (1 YEAR) OF 107 PATIENTS (OUT OF 139 OPERATED IN 1957) WHO HAD AN 80% TO 100% FUNCTIONAL OPENING AFTER THE "CREATION OF A SEPTAL LEAFLET"

Condition:	Excellent	Good	Fair	Unchanged	"Worse"
No. of Patients	31	62	9	1	4
Percentage	29	58	8	1	4

respects. While the valve is still very tight, practically any effort to enlarge the opening leads to its complete obstruction and momentarily interrupts the cardiac output. Although the surgeon consciously tries to avoid blocking the orifice for more than three consecutive heart beats, this manipulation nearly always is associated with at least momentary disappearance of the peripheral pulse and blood pressure. Secondly, even in the absence of obstruction to the blood flow by the operating finger the application of pressure to the valve very frequently has a markedly deleterious effect upon the ventricular contractions (perhaps by reflex effect), at times producing momentary asystole, extrasytoles, or ventricular tachycardia, with resulting severe drop in blood pressure. In younger individuals in whom the left ventricle is in good condition, the heart beat and the blood pressure return to normal within a matter of seconds. In the older individual and in patients with more advanced cardiac pathology (poorer myocardium) on the other hand, the momentary myocardial failure may initiate a vicious circle in which the diminution in cardiac output and the low blood pressure cause an impairment in the perfusion of the coronary arteries which in turn tends to perpetuate the left ventricular failure. It is nothing short of remarkable that frequently the myocardium even under such unfavorable conditions does regain its strength so that the patient manages to leave the operating table in good condition. Not infrequently, however, acute myocardial failure, pulmonary edema, severe hypotension, ventricular fibrillation, or frank cardiac arrest may supervene. Naturally, the inadvertent creation of a significant amount of valvular incompetence by increasing the left ventricular work load will aggravate the tendency toward such acute failure.

Patients in extremely poor condition preoperatively may develop cardiac arrest during the induction of anaesthesia or during the opening of the chest. Such was the case with the two patients who died prior to any definitive surgical manipulation.

2. In other cases, although the valve is opened satisfactorily and without any untoward circulatory incident during the definitive manipulations, the left ventricle and left atrium become noticeably distended shortly after repair of the cardiotomy wound. In some instances the pressure within the left atrium has been measured at 50 mm. of mercury or more. Acute pulmonary edema usually supervenes, although cardiac arrest or ventricular fibrillation may precipitate complete circulatory failure before there is time for pulmonary edema to develop. On one such occasion it was demonstrated that thrusting a scalpel blade through the interatrial septum, thus creating a small interatrial septal defect to decompress the distended left atrium, can be life-saving (Fig. 15). Indeed, the prompt disappearance of the signs of pulmonary congestion and the immediate improvement in the vigor of the contractions of the left ventricle in such circumstances is most dramatic. Although a vigorous continuous thrill often may be palpated immediately over a localized area of the right atrial wall, postoperative catheterization has revealed that the left-to-right shunt through the septal defect becomes reduced progressively and disappears within three months (in all but one of our patients). There exists considerable experimental evidence (Swan et al),[21]

which suggests that atrial septal defects created artificially will not remain open unless an area of 1.5 cm. in diameter or more has been excised.

It would seem that the surgical relief of the obstruction at the mitral valve permits a suddenly increased influx of blood into the relatively "atrophied" and unprepared left ventricle which this chamber may not be capable of dealing with from one beat to the next. The resulting dilatation of the ventricle may impair its contractability to a most dangerous extent. While, conceivably, a less adequate enlargement of the valve would enable us to avoid the risk of this complication, such limitation of the operative relief of the obstruction would hardly be in the patient's interest in the long run. A method for reducing the acute load upon the left side of the heart both before an effective opening of the valve as well as immediately after such a procedure would be provided by elective creation of an interatrial septal defect. Such a procedure was, in fact, suggested as a partial surgical treatment in the earlier stages of mitral stenosis surgery.[22,23] However, it does not contribute, of course, by itself to the actual relief of the valvular obstruction.

MECHANICAL SUPPORT OF THE CIRCULATION

Total Heart-Lung Bypass — Open-Heart Technique

A more definitive way of providing support for the left ventricle during operation would involve the utilization of a circulatory bypass system which would divert either the whole, or at least an important part of the blood stream from the heart for the duration of the surgical procedure. Many very excellent cardiac surgeons favor complete "open-heart" procedures for mitral stenosis[24] since from the point of view of good physiological and surgical principles such total support for the organ on which an operation is being performed is very much in place. The advantages of being able to "see" the lesion would seem to be obvious. Indeed, we now have come to use the open technique as a preferred routine for mitral stenosis. By opening the left atrium widely (using a left thoracic approach) such excellent exposure of the valve is provided that an ideal type of "neostrophingie" mobilization may be accomplished in practically every patient. At least we may confidently expect to overcome the stenosis completely without risk of producing incompetence. Any associated regurgitation may be relieved simultaneously. Nevertheless, chiefly because of logistical problems, many cases must be operated "closed."

Closed Technique with Left Ventricular Bypass

It has been possible to apply a rather simple method of bypass support of the left ventricle during the course of the operation which does not require the use of additional quantities of blood or an open technique, and at the same time serves to establish, at the conclusion of the procedure, a balancing but slowly closing atrial septal defect. Since the patient's own lungs nearly invariably are capable of providing full oxygenation of his circulating blood and since there is relatively little danger of right-sided heart failure during the surgical procedure itself, in the usual case of mitral stenosis the circulation may be supported adequately by withdrawing (subtotally) oxygenated blood from the left atrium (after total bodily heparinization) and returning it to the sys-

temic arterial tree by way of one of the peripheral arteries (usually the left femoral artery). The left atrial cannulation can be accomplished through the standard right anterior thoracic incision. A Bardic catheter (generally size 26 or 28 F) on a pointed obturator, pierces the right atrial appendage through an area secured by a pursestring suture, enters the right atrium and, with the help of the sharp point penetrates the muscular portion of the atrial septum to enter the left atrial cavity. (Fig. 16AB). The tubing and arterial catheter used for this simple bypass system is prepared and autoclaved in packaged form. After cannulation of a femoral artery, the patient's own blood is used to displace all air through the combined air and fibrin trap (Fig. 17). When all is in readiness the rubber midportion of the bypass line is placed within the head of a finger pump* and the bypass is started. The bypass flow is increased to a level which is one-half to three-fourths of the estimated cardiac output. By permitting the left atrium to contain some blood, it is prevented from collapsing upon the finger, and no tendency toward aspiration of air into the heart will occur in case the instrument and finger should fail to tamponade the atrial incision perfectly at all times. It was amazing to us to observe that a jet of regurgitation from the mitral valve, when present, does not seem to weaken or diminish appreciably (to palpatory evaluation) when the estimated transmitral blood flow is reduced by the bypass to as little as 500 cc. per minute. Thus, this very valuable sign of the state of valvular competence is maintained during optimal operating conditions.

Once the bypass has been established at a suitable rate the operator may attack the valve without having to worry about interference with the transmitral blood flow, the production of a severe drop in arterial blood pressure, or transient cardiac irregularities. Careful monitoring of the vital functions, particularly the systemic blood pressure, is, of course, practiced throughout the time of the bypass.

Thus, proceeding systematically and without the usual necessity for frequent interruptions in the definitive surgery the valve can be mobilized methodically to the desired extent. Upon completion of the intracardiac manipulations the finger is withdrawn from the heart and the cardiac wound of entrance is repaired. The pump is slowed down, gradually permitting the left ventricle to take over more and more of the circulatory load. When the bypass has been terminated, the left atrial catheter is removed from the heart, leaving open the small interatrial septal defect. The femoral catheter is removed and the arterial incision is sutured. Polybrene* is administered to neutralize the heparin, as recommended by Weiss et al.[43] Total operative blood loss (skin-to-skin) including requirements of the bypass in these cases has averaged less than 1500 cc.

Closed Technique with Total or Subtotal Cardiopulmonary Bypass

In patients in the latest stages of the disease in whom the right ventricle is functioning under adverse conditions due to chronic failure, tricuspid insufficiency, or extreme pulmonary hypertension simple left

*Obtainable from Sigmamotor Co., Middleport, N. Y.
*Hexadimethrine Bromide. Obtainable from Abbott Laboratories, North Chicago, Illinois.

ventricular bypass may not suffice. In these cases it may be advisable to bypass both sides of the heart during the surgical manipulations. This is best done with the help of a conventional oxygenator bypass, the blood being collected by a wide bore multiwindowed plastic catheter from the right atrium, passed through the oxygenator, and returned as arterial blood to the peripheral circulation.* The operative procedure, under such conditions usually will be performed as a closed technique since such extremely ill patients are not favorable candidates for an "open" procedure. However, should it become advisable to open the left atrium widely for some reason (such as the presence of massive intratrial thrombosis), this may be done readily.

*In this fashion both ventricles are supported during the course of the definitive manipulations.

Comment

While the technique of subtotal bypass of the left ventricle and the creation of an interatrial septal defect of small size was employed at first only in those patients who were considered to be critically ill, we have gradually come to use it in nearly all patients operated for mitral stenosis by a closed technique. Since no more blood is required with this type of bypass operation than in closed conventional procedures for mitral stenosis and since there have been no serious bleeding problems associated with the use of these relatively short periods of bypass (average 24 minutes), it would seem that no patient should be deprived of the advantages of assurance of a stable blood pressure, adequate cardiac output, and efficient coronary perfusion while the operator is entirely freed from the psychological stresses which otherwise might cause him to perform an operation of less than ideal extensiveness, or worse, to carry out hasty and extremely dangerous maneuvers upon one of the most delicate and important structures in the human body.

None of the 462 patients reported herein were the beneficiaries of such circulatory support. A more recently compiled series of patients so supported during surgery is presently under review. A very significant improvement both in the operative accomplishment and in the rate of survival has become apparent and will be presented in a future communication. However, further perfection in the techniques of complete circulatory bypass and in "open-heart" procedures for mitral stenosis have led to great improvements in accomplishment and in safety. As a result, we have finally come to prefer this method of handling for nearly every case.

SUMMARY

The surgical treatment of mitral stenosis has developed in the short span of a decade from a basically unsatisfactory palliative operation to one which now holds out the hope for a complete cure for the great majority of patients with this lesion.

This is the result of a careful re-appraisal of the anatomical, pathological and physiological aspects of mitral stenosis together with the practical experience gained from thousands of cases.

The new operation aims at the creation, de novo, of a mobile septal leaflet out of the usually irretrievably mutilated mitral valve. To achieve optimal results and a minimal operative mortality rate, it has been found advisable to support the systemic arterial circulation during the operative procedure by a left ventricular bypass, and to leave a small atrial septal defect post-operatively to permit the possibility of temporary decompression of the left atrium whenever necessary.

The open technique of surgery for mitral stenosis finally has become the operative method of choice in most patients, since it carries basically no greater risk and offers many advantages, particularly in very severely damaged valves.

RESUMEN

El tratamiento quirúrgico de la estenosis mitral, se ha desarrollado en el corto intervalo de 10 años desde la operación básica, paliativa no satisfactoria hasta una que ahora mantiene las esperanzas de obtener una curación completa para la mayoría de los enfermos.

Este es el resultado de una revaluación cuidadosa de los aspectos anatómicos, patalógicos y fisiológicos de la estenosis mitral unidos a la experiencia práctica que se ha ganado en millares de casos.

La nueva operación se orienta hacia obtener la creación como cosa nueva de una hojilla móvil septal derivada de la válvula mitral habitualmente inutilizable. Para lograr resultados óptimos y una mortalidad operatoria mínima recientemente se ha encontrado aconsejable soportar la circulación general durante el procedimiento opera-

torio, mediante una desviación ventricular izquierda y dejar un pequeño defecto septal atrial postoperatoriamente para permitir la posibilidad de decompresión temporal del atrio izquierdo cuando sea necesario.

Si bien la experiencia con esta desviación se limita a poco más de 100 enfermos, parece evidente que su superioridad es mucho mayor a los procedimientos anteriores para la estenosis mitral en la gran mayoría de los enfermos operados por medio de cirugía "cerrada." El procedimiento de cirugía abierta para estonosis mitral al fin ha llegado a ser el método operativo preferido para la mayoría de los enfermos debido a que básicamente no presenta un riesgo mayor y en cambio ofrece muchas ventajas especialmente en casos de válvulas seriamente dañadas.

RESUMÉ

Le traitement chirurgical de la sténose mitrale s'est développé dans le court espace d'une décade, en partant d'une opération palliative par essence insatisfaisante, pour aboutir à celle qui apporte l'espoir d'une guérison complète pour la grande majorité des malades atteints de cette lésion.

C'est le résultat d'une soigneuse réestimation anatomique, pathologique et physiologique de la sténose mitrale associée à l'expérience pratique apportée par des milliers de cas.

La nouvelle opération tend à la création d'un nouveau volet mobile en dehors de la valvule mitrale généralement mutilée d'une façon irréversible. Pour obtenir des résultats optimum et un taux de mortalité opératoire minimum, récémment on a trouvé opportun de renforcer la grande circulation artérielle pendant le temps opératoire, par un court-circuit du ventricule gauche et de laisser un petit pertuis de la paroi de l'oreillette après l'opération pour permettre la possibilité d'und décompression temporaire de l'oreillette gauche en cas de nécessité.

L'expérience de cette opération avec le court-circuit ess limitée pour le moment à un peu pius de 100 malades. Toutefois il semble évident que son efficacité sera de loin supérieure pour la grande majorité des malades dont, l'ancienne méthode "l'operation fermée" du coeur est indiquée.

Les progrès actuels de l'extracorporal machine nous permet une operation ouverte du coeur pour la correction du stenose mitral qui est le procéde de choix. Cette operation nous donne une complète restitution de la fonction valvulaire sans augmenter la mortalité operatoire.

ZUSAMMENFASSUNG

Die chirurigsche Behandlung der Mitralstenose wurde in der kurzen Zeitspanne eines Jahrzehntes entwickelt aus einer im Grunde unbefriedigenden palliativen Operation zu einer solchen, die heute die Hoffnung auf eine komplette Heilung der Mehrzahl solcher Kranken begünstigt.

Diese chirurgische Behandlung ist das Resultat einer sorgfältigen und erneuten Auswertung anatomischer, pathologischer und physiologischer Erhebungen über die Mitralstenose zusammen mit der an Tausenden von Fällen gewonnenen praktischen Erfahrungen.

Das neue operative Vorgehen erstrebt von neuem die Schaffung eines mobilem Segels aus der für gewöhnlich irreparabel verstümmelten Mitralklappe. Kürzlich erst hat es sich, um optimale Resultate und eine möglichst garinge Sterblichkeitsziffer zu erzielen, als ratsam erwiesen, den arteriellen Körperkreislauf während der operativen Phase durch einen Kurzschluß den Ventrikels zu unterstützen und postoperativ einen kleinen Vorhofscheidewanddefekt zu belassen, um im Notfall die Möglichkeit einer temporären Entspannung des linken Atriums zu haben.

Während sich die Erfahrung dieser durch einen Kurzschluß unterstützten Operation auf wenig mehr als 100 Patienten stützt, liegt es offen zu Tage daß ihre Wirksamkeit für die Mehrzahl der Patienten, die nicht mit offener herzchirurgischer Technik behandelt werden.

Im Lichte der Fortschritte in den Methoden der offenen Herzchirurgie finden wir dass fuer die meisten Faelle von Mitralstenoose die offene Technik angebracht ist. Diese ermoeglicht vollkommene Restitution der Klappe ohne erhebliche Erhoehung des Risikos.

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Aneurysm of the Ascending Aorta with Obstruction of the Superior Vena Cava: Report of Case with Resection Using Extracorporeal Circulation*

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Recent surgical advances, including the ability to bypass the heart and lungs, have made possible resection of the ascending aorta for aneurysms. The bleak outlook for patients with untreated thoracic aneurysms has been properly stressed by many authors since the classic articles of Lemann[1] in 1916 and Boyd[2] in 1924. Resections for aneurysms of the ascending aorta prior to the introduction of the heart-lung bypass technic were limited to tangential resection of the aorta and aorotorrhaphy for saccular aneurysms with narrow necks and relatively healthy adjacent aortic walls.[3,4] De Bakey and associates[5,6] demonstrated the technical feasibility of resection of the ascending aorta for fusiform aneurysms with the aid of extracorporeal circulation. Reports of two successful attempts done by this group appeared in the literature in 1956 and 1957.

The present report is that of a patient having a large fusiform aneurysm of the ascending aorta which had ruptured to form an additional false aneurysm in the anterior mediastinum. The presence of these two masses caused the rather uncommon complication of compression and obstruction of the superior vena cava.

Report of Case

A 62-year-old white man was hospitalized immediately on admission to the Mayo Clinic on May 27, 1959. He was referred because of pain in the right side of the thorax of 4 months' duration and swelling of the face and neck for 6 weeks. He had been well except for a painful right shoulder diagnosed and treated as pariarthritis by the physician in his home locality in October, 1958. A roentgenogram of the thorax at that time showed only slight tortuosity of the ascending aorta. During January, 1959, the patient had begun to have dull intermittent pain in the right anterior and lateral part of the thorax, which became more severe in the following 4 months. The pain was located in the region of the third to the eighth ribs on the right from the mid-clavicular line anteriorly to the mid-scapular line posteriorly and was not related to exertion, position, breathing, coughing or sneezing.

During mid-April, 1959, he noted the onset of swelling and a dusky cyanosis of his face and neck most noticeable after lying down for long periods. The size of his collar had increased from 14½ to 16 inches during the 6 weeks before admission. He had had blurring of his vision on arising in the mornings, but no headaches. A dry cough, slight huskiness of his voice, dyspnea after walking up half a flight of stairs, and occasional paroxysmal nocturnal dyspnea had developed in the 6 weeks prior to admission. On May 26, a roentgenogram of his thorax had revealed a mass, and he was referred with the presumptive diagnosis of a neoplasm.

On examination the patient appeared well-developed, well-nourished and younger than his stated age. His face, neck and upper part of the thorax appeared puffy and suffused with a dusky cyanosis. Both jugular veins were markedly distended, and many collateral veins could be seen on the anterior chest wall. Superficial venous stars were evident along the costal margins. Veins in the arms showed increased venous pressure. The veins of the right arm collapsed at 60 degrees from the horizontal and those of the left arm at 90 degrees. Blood pressure was 118 mm. Hg systolic and 70 diastolic in both arms; radial pulses were 64 beats per minute and were equal in amplitude; the oral temperature was 98.6° F. A slight tracheal tug, without any shift of the trachea, was evident. Percussion dullness and a systolic, pulsating prominence of the right pectoral area were present over the second through

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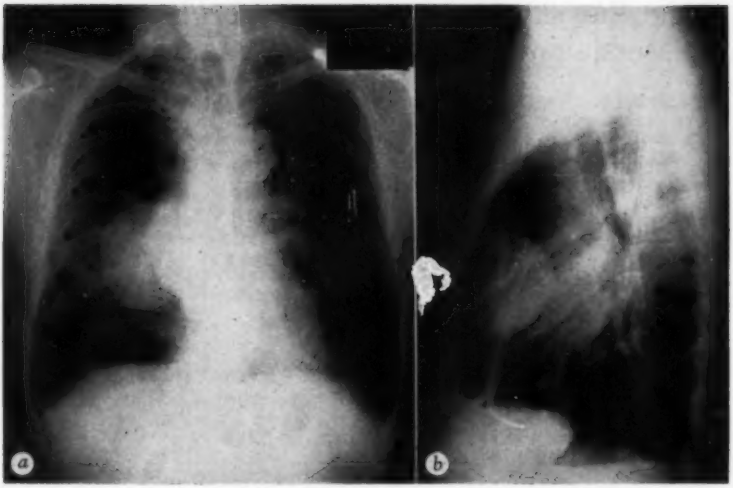

FIGURE 1: The thorax. *a*. Posteroanterior view demonstrating an aneurysm of the ascending aorta and the more lateral mass formed by the false aneurysm. *b*. Lateral view demonstrating the false aneurysm with its broad base lying against the anterior chest wall.

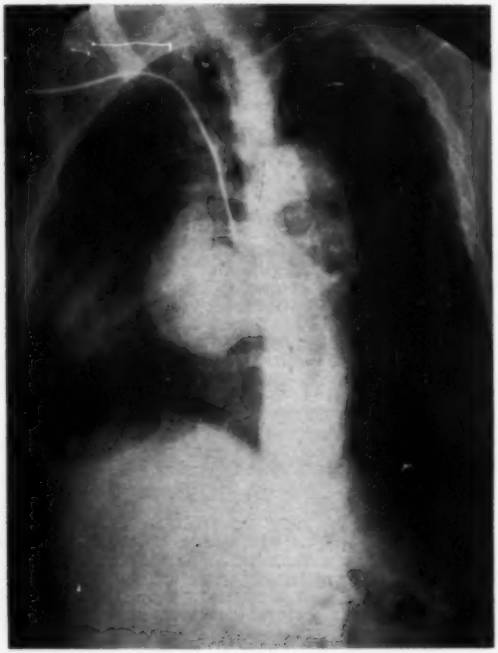

FIGURE 2: Aortogram demonstrating the catheter in the ascending aorta, the large fusiform aneurysm filled with contrast medium, and the false aneurysm that did not fill with the contrast medium.

the fifth ribs anteriorly. Heart tones were clearly audible in the area of dullness giving the erroneous initial impression of a dextrocardia. The second cardiac sound had a woody quality and was narrowly split. With the patient in the sitting position, a faint diastolic bruit was heard in the right upper anterior portion of the chest. There was no evidence of aortic incompetence.

Laboratory examinations revealed 9300 leukocytes per cubic millimeter of blood, a normal differential count except for 8 per cent eosinophils, 13.8 gm. of hemoglobin per 100 ml., a sedimentation rate of 55 mm. in 1 hour (Westergren method), 36 mg. of urea per 100 ml. of blood and positive Wassermann, Hinton and Kahn reactions. The Kahn reaction was 4 plus with 1024 units. (The patient denied previous knowledge of syphilitic infection). Urinalysis was normal except for 6 erythrocytes and 3 pus cells per high-power field. The electrocardiogram was normal. Roentgenograms and fluorograms of the thorax (fig. 1) revealed a distinct globular anterior mediastinal mass attached to the anterior chest wall beneath the right costosternal border at the level of the third and fourth intercostal spaces. A separate mass situated more posteriorly suggested an aneurysm of the ascending aorta. A retrograde aortogram revealed a large aneurysm of the ascending aorta extending down to the aortic sinuses. The right anterior mass was not filled with opaque media and appeared to be separate from the aneurysm (fig. 2).

The patient returned on June 26, 1959, for surgical excision of his aneurysm. He had no new symptoms, but he complained of increased pain in the right anterior portion of the thorax and in the right arm, and of increased puffiness of the face. During the interim he had received a course of 10,000,000 units of penicillin as the first and only known treatment for the syphilitic infection prior to operation.

On July 1, 1959, resection of the ascending aortic aneurysm was performed. Extracorporeal circulation and intermittent perfusion of the coronary artery were used in the course of the operation. A woven (teflon) aortic prosthesis was inserted as the aortic graft. The operation proceeded as follows: The right external iliac was exposed extraperitoneally. Primary median sternotomy was done, and extensive venous bleeding due to the obstruction of the superior vena cava was encountered. The aneurysm was located to the right of the sternum and was intimately adherent to the anterior chest wall. It began just above the aortic valve but did not include the sinuses of Valsalva. A "false" aneurysm originated from its anterolateral surface and extended to the right anterior part of the chest wall. This false aneurysm later was found to be filled with clotted blood.

Extracorporeal circulation was instituted after the right external iliac artery and the right atrium were cannulated. A tape was placed about the pulmonary artery and was used to occlude this vessel as complete heart-lung bypass was instituted. Circulation to the head and upper part of the trunk was maintained satisfactorily by retrograde aortic flow. The aorta was cross-clamped just proximal to the innominate artery. The fusiform aneurysm was excised, and a tubular, woven (teflon) prosthesis 1¼ inches in diameter was sutured in place in the aorta. The posterior half of the lower anastomosis was accomplished first, then the upper anastomosis and, finally, the anterior half of the lower anastomosis. After 15 minutes of cardiac asystole, the left coronary artery was perfused for 5 minutes. This was repeated after a second 15-minute period of asystole. The coronary cannula was withdrawn as the anastomosis was rapidly completed; and the prosthesis was allowed to fill with blood. The constrictions of aortic and pulmonary arteries were released, and excellent cardiac action was maintained. Protamine was given, and bleeding at the anastomotic sites was controlled gradually. There was no bleeding through the prosthesis itself. The cannulae were removed, and the external iliac artery was repaired. The clot filling the false aneurysmal sac was scooped away with the hand, leaving most of the thin wall intact. The sternum was reapproximated with four encircling steel-wire sutures, and the remaining layers were sutured with silk. Temporary bilateral closed drainage of the chest was instituted.

The pathologist reported that the resected tissue was an "aneurysm in pieces, partially filled with laminated thrombus," and that there was marked chronic inflammation, probably syphilitic in origin.

The postoperative course was uncomplicated, and the patient was dismissed 15 days after operation. His only complaints were slight numbness of the ring and fifth fingers of his left hand. He had no bruits, murmurs or other abnormal findings except absence of pulses in the ulnar artery and reduced pulses in the radial artery on the right resulting from the retrograde aortogram. All signs of obstruction of the superior vena cava had disappeared. A roentgenogram of the thorax revealed a normal aortic shadow.

Comment

The classic triad of symptoms of a thoracic aortic aneurysm, all three of which were present in the case just reported, are cough, present in 73 per cent of cases, dyspnea, in 70 per cent, and pain, in 67 per cent, according to Cranley and associates.[2] Other common symptoms are dysphasia, loss of weight, anorexia and palpitation. Signs that may be present on examination are an area of dullness and abnormal pulsations over the aneurysm, a delay in one radial pulse, inequality of the pupils from irritation of the superior cervical sympathetic nerves, tracheal tug, a dull or woody first heart sound, a loud ringing type of second aortic sound, the signs of

aortic regurgitation, a bruit, and an obstructive type of bronchial sounds. A humming-top murmur may be heard if the aneurysm has ruptured into the nearby pulmonary artery[8,9] or vena cava. Congestive heart failure, compression of the pulmonary artery or major veins and cyanosis are occasional effects of large aneurysms.

Cranley and associates,[7] in 1954, reported on a series of 230 aneurysms encountered at necropsies performed between 1926 and 1952. In this series, 189 aneurysms (82 per cent) were syphilitic, 32 (14 per cent) arteriosclerotic, three (1.3 per cent) a combination of the two, five (2.2 per cent) were the result of mycotic infections, and one (0.4 per cent) was due to trauma. From 1926 to 1930 the incidence of syphilitic aneurysms in their series was one in 46 necropsies whereas from 1946 to 1950 it had dropped to one in 201 necropsies. The majority of recent reports on aneurysms show that arteriosclerosis is the most frequent cause of aneurysms. Eighty-nine per cent (169 cases) of the 189 syphilitic aneurysms in the series reported by Cranley and his associates[7] were in the thoracic aorta and 11 per cent (20 cases) were abdominal. Eighteen of these 20 abdominal syphilitic aneurysms were located above the renal arteries. The vast majority (78 per cent) of the syphilitic thoracic aneurysms were found in the ascending aorta or the arch. Arteriosclerotic aneurysms, on the other hand, appear most commonly in the abdomen below the renal arteries. Twenty (62 per cent) of the 32 arteriosclerotic aneurysms in the series reported by Cranley and associates were in this location. Of the 12 thoracic arteriosclerotic aneurysms in their series, 10 were located in the distal portion of the arch or descending aorta.

De Bakey and associates,[10] in 1958, reported on 50 aneurysms of the aortic arch resected by the various available technics including extracorporeal circulation. The mortality rate in this series was 56 per cent. Factors favoring a high mortality rate were the age (especially an age of 60 years or more), a fusiform type of aneurysm, and arteriosclerosis as the etiologic agents. This high mortality rate, based on a relatively small number of cases, must be compared to the extremely high mortality rate from the untreated aneurysm. In 633 cases of saccular thoracic aneurysms Kampmeier[11] stated that the average life expectancy after onset of symptoms was 6 to 9 months. Cranley and associates found that of 230 patients with untreated thoracic aneurysms, 59 per cent had died in 1 year, and 77 per cent in 2 years following onset of symptoms.

The complications of thoracic aneurysms are those of compression of nearby vital structures and of rupture. Cranley and associates gave statistics for 90 thoracic aneurysms causing compression or rupture; only one caused compression of the superior vena cava and one other ruptured into the superior vena cava. Compression of trachea, bronchus, lung and pulmonary artery, or rupture into the esophagus, pericardium, pleura, and pulmonary artery are considerably more common than is the syndrome of superior vena caval compression.

In an analysis of the causes of 274 cases of superior vena caval obstruction, Schechter[12] found aortic aneurysms were second only to carcinoma as the most common cause. Seventy-seven (28 per cent) of the cases of the syndrome of superior vena caval obstruction were caused by aneurysms. However, in only one of Schechter's last 22 cases of superior vena caval syndrome, and in none of the 33 cases reported by Failor and associates in 1958,[13] was aneurysm the etiologic agent. A more nearly accurate estimate of the frequency of aneurysms as the cause of compression of the superior vena cava within the past 5 to 10 years is less than 2 per cent.

SUMMARY

A large fusiform aneurysm involving the entire ascending aorta was successfully excised with the aid of extracorporeal circulation. Prior to operation the patient had a pulsating mass on the anterior chest wall, and presented an unusual roentgenographic picture caused by a large clot-filled false aneurysm which had arisen from a ruptured syphilitic fusiform aneurysm. Following excision of the aneurysm and resection of the aorta, the superior vena caval compression syndrome disappeared and the patient was able to return to normal activity after an uncomplicated convalescence.

RESUMEN

Se resecó un gran aneurisma fusiforme que incluía totalmente la aorta ascendente, con buen resultado, con la ayuda de la circulación extracorpórea.

Antes de la operación, el enfermo tenía una masa pulsátil en la pared anterior del tórax y presentaba un aspecto radiológico inusitado causado por un falso aneurisma lleno de coágulos que se había desarrollado a partir de la ruptura de un aneurisma sifilítico fusiforme. Después de la excisión del aneurisma y de la resección de la aorta, el síndrome de compresión de la vena cava superior desapareció y el enfermo fué capaz de volver a la actividad normal después de una convalescencia sin complicaciones.

RESUMÉ

Un volumineux anévrysme fusiforme comprenant l'aorte ascendante dans sa totalité a été extirpé avec succès grâce à la circulation extra-corporelle. Avant l'opération, il existait une masse battante sur la paroi thoracique antérieure du malade. Le tableau radiologique étant inhabituel, il était dû à un volumineux pseudo-anévrysme empli de caillots qui était apparu à la suite de la rupture de l'anévrysme syphilitique

fusiforme. Après exérèse de l'anévrysme et résection de l'aorte, le syndrome de compression de la veine cave supérieure disparut et le malade fut en état de reprendre une activité normale après une convalescence sans complications.

ZUSAMMENFASSUNG

Ein grosses spindelförmiges Aneurysma, das die ganze aufsteigende Aorta betraf, wurde mit Hilfe des extracorporalen Kreislaufes erfolgreich exzidiert. Vor der Operation hatte des Patient eine pulsierende Masse an der vorderen Brustwand und bot ein ungewöhnliches Röntgenbild infolge eines grossen, mit einem Thrombus gefüllten falschen Aneurysmas, das von einem rupturierten syphilitischen spindelförmigen Aneurysma entstanden war. Nach der Exzision des Aneurysmas und Resektion der Aorta bildete sich das Kompressions-Syndrome der oberen Hohlvene zurück, und der Patient war imstande, nach einer komplikationslosen Rekonvaleszenz seine normale, aktive Lebensweise wieder augzunehmen.

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Proposal of a Method for Estimating Bronchial Blood Flow by Simultaneous Measurements of the Left and Right Ventricular Outputs with the Dye Dilution Technique*

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Although the measurement of bronchial blood flow has been greatly desirable for investigating the bronchial circulation in human subjects, the method available for it has been scarcely published. In 1947, for the first time, Bing, Vandam and Gray[1,2] reported a method for measuring the collateral circulation of the lungs in congenital heart diseases, in which the pulmonary circulation is thought to consist chiefly of bronchial blood. Improving this method, Nakamura[3] in 1956 reported a study on the bronchial circulation in silicosis. After that, Nakamura, Takizawa and Katori[4] also measured an increased bronchial blood flow in other pulmonary diseases by using the same method. However, the method was quite time-consuming, and operator's specific skillfulness, as well as the subject's close cooperation were indispensable for the measurement. Consequently, it frequently produced unexpected analytical errors and often did not exhibit adequate reproducibility.

Under the development of the bronchial arteries, the output of the left ventricle is to be more than that of the right by the value of bronchial blood flow, for the bronchial blood, arising from the aorta, immediately returns to the left atrium through the pulmonary capillaries and veins without first passing to the right side of the heart. Accordingly, when the outputs of the left and right ventricles can be measured separately, the difference between the two outputs is to be blood flow through the bronchial arteries. In 1957, the authors[5] reported the experimental studies for measuring bronchial blood flow, which consist of simultaneous measurements of the outputs of the left and right ventricles with the dye dilution technique. The same year, Fritts, Harris, Chidsey, Clauss and Cournand[6] reported a method for measuring the output of the right ventricle and suggested a possibility to determine the bronchial blood flow in its application.

The purpose of this paper is to propose a method for measuring bronchial blood flow, and to validate this method by three experimental approaches: 1) measurements of the outputs of both the ventricles in healthy persons, 2) the same measurements in normal dogs and 3) experiments in dogs with left subclavian-pulmonary anastomosis.

Methods and Materials

Under fluoroscopic guidance, one cardiac catheter was introduced into an antecubital vein and advanced until the tip lay in the main

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pulmonary artery. Another catheter was then advanced through a second vein until its tip lay in the superior vena cava. A Cournand needle was inserted into the brachial artery. Three to 4 cc. of 0.5 per cent Evans blue or 5 per cent bromsulphalein were rapidly injected into the superior vena cava through the latter catheter. Simultaneously, blood was sampled in small test tubes from the pulmonary artery and brachial artery every one second. For the blood sampling from the pulmonary artery through the catheter, a No. 9 cardiac catheter was usually used because of more facile flow of blood. The end of the bleeding catheter was inserted into a negative pressure chamber evacuated to a pressure of approximately 200 mm Hg. below atmospheric. In this way, the rate of flow through the catheter was approximately 1.5 cc. per second and the blood was collected in small cells placed on the circumference of a synchronous revolving drum which was located inside the evacuated chamber. Blood sampling from the brachial artery through the Cournand needle was performed under atomospheric pressure.

Dye concentration in serum was measured by the electrophotometer at the wave-length of 610 mμ for Evans blue and 570 mμ for bromsulphalein and two dye dilution curves, from the pulmonary artery and brachial artery, were inscribed on semi-logarithmic paper. Cardiac output, according to Hamilton et al.,[7] was calculated as follows:

$$C.O. = \frac{60\ I}{C\ T} \times \frac{100}{(100 - Ht)}$$

where C.O. is cardiac output (1/min.), I dye injected (mg.), C average dye concentration in serum in dye dilution curve (mg/l), T passage time (second) and Ht hematocrit of blood.

The output of the left ventricle can be determined by the dye dilution curve drawn from the brachial artery. By the same reasoning, the curve drawn from the pulmonary artery should determine the out-

TABLE 1 — LEFT AND RIGHT VENTRICULAR OUTPUTS IN HEALTHY PERSONS

Subject	Sex	Age	Body Surface Area	L.V.O.	R.V.O.	L.V.O. — R.V.O.	$\frac{\text{L.V.O.} - \text{R.V.O.}}{\text{R.V.O.}} \times 100$
			M^2	1/min	1/min	1/min	Per cent
S.Y.	M	45	1.77	8.15	8.71	— 0.56	— 6.4
G.S.	M	40	1.62	6.82	7.29	— 0.47	— 6.4
F.T.	M	30	1.58	6.58	6.80	— 0.22	— 3.2
Y.A.	M	31	1.71	6.87	6.81	0.06	0.9
A.S.	M	24	1.67	10 39	10.38	0.01	0.1
				10.02	9.79	0.23	2.3
Y.T.	M	26	1.51	5.53	5.46	0.07	1.3
				5.70	5.61	0.09	1.6
T.K.	M	39	1.54	6.55	6.13	0.42	6.9
H.T.	M	36	1.51	6.30	6.27	0.03	0.5
B.C.	M	41	1.49	6.94	6.11	0.83	13.4
A.K.	F	21	1.41	7.28	7.93	— 0.65	— 8.2
I.S.	M	20	1.74	7.97	7.85	0.12	1.5
Mean				7.32	7.32	0.00	
S.D.				± 1.45	± 1.49	± 0.38	

L.V.O. = Left Ventricular Output
R.V.O. = Right Ventricular Output

put of the right ventricle. When the dye dilution curve was plotted using a lineal scale for the time and a logarithmic scale for dye concentration, the downslope of the curve from the pulmonary artery constantly formed a straight line same as that from the brachial artery and appearance of recirculated dye on the former generally occurred in the lower part of the downslope than on the latter. However, when dye was injected into the peripheral veins, the downslope of the curve from the pulmonary artery was frequently found to form an irregular line, so that the calculation of cardiac output was impossible, as Fritts et al.[6] stated. For the measurement of the right ventricular output, therefore, it was indispensable that dye was injected into the vena cava through the cardiac catheter.

In experiment 1, the outputs of the left and right ventricles were measured in eleven healthy persons, nine of whom were frequent blood donors who sometimes were found to be anemic. All were studied under basal condition without taking a meal at least three hours before the experiment.

In experiment 2, the same procedures were performed in nine normal adult dogs weighing from 8 to 35 kg., anesthetized intravenously with pentbarbital sodium (about 30 mg/kg).

In experiment 3, five dogs were anesthetized with pentbarbital sodium and received thoracotomies at the left third or fourth intercostal space under artificial pressure oxygen breathing with an endotracheal tube, and between the left subclavian artery and left pulmonary artery a bubble flow-meter was connected with two tubes which are 3 mm. in inner diameter, 30 cm. in length. At the subclavian side of the connection, a mercury manometer was fitted up to record and control blood pressure. In this situation, in which arterial blood was directly flowing into the left lung through the subclavian-pulmonary connection, the left and

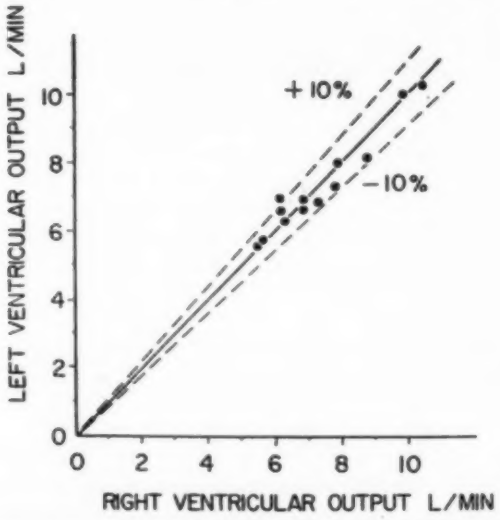

FIGURE 1: Comparison of left ventricular output and right ventricular output in healthy persons.

right ventricular outputs were measured, and simultaneously blood flow through the connection was determined by the bubble flow-meter. Immediately, the connection was cut off at its pulmonary side and the bleeding volume from the connecting tube was measured for 15 seconds.

Results

Experiment 1. The results of the left and right ventricular outputs simultaneously measured in eleven healthy persons are shown in Table 1 and Figure 1. In all cases but one with the difference of + 13.4 per cent, the right ventricular output was agreed with the left within ± 10 per cent. The mean value for both the outputs was 7.32 l/min ± 1.45 and 1.49 respectively. The mean difference between the two values was 0.00 ± 0.38.

Experiment 2. In Table 2 and Figure 2, it can be seen that the left and right ventricular outputs show an extremely close correlation in 12 measurements in nine normal dogs. The differences between the two outputs were less than ± 10 per cent of the right output in all cases but one and less than ±5 per cent in one-half. In this series, the mean left and right outputs were 2.27 lit/min and 2.29 lit/min, with standard deviations of 1.43 and 1.42 respectively. Here the difference was 0.02 ± 0.16.

Experiment 3. The left and right ventricular outputs measured by the dye dilution method and the values of shunted blood flow determined by the bubble flow-meter and bleeding method in five dogs with the subclavian-pulmonary anastomosis are shown in Table 3. In all cases the outputs of the left ventricle showed higher values than those of the right and the difference between the two outputs corresponded roughly with the values obtained directly by both the flow-meter and bleeding method.

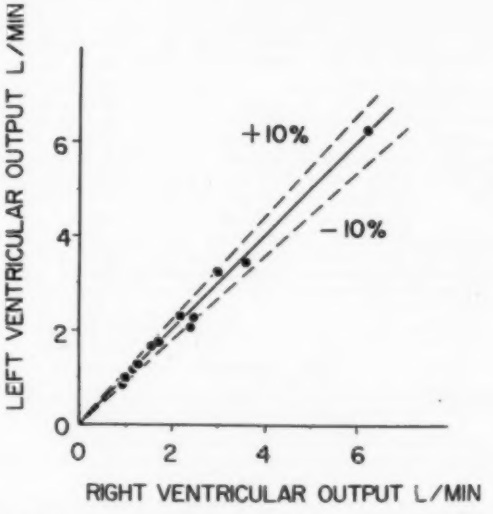

FIGURE 2: Comparison of left ventricular output and right ventricular output in normal dogs.

TABLE 2 — LEFT AND RIGHT VENTRICULAR OUTPUTS IN NORMAL DOGS

Dog No.	Body Weight	L.V.O.	R.V.O.	L.V.O. — R.V.O.	$\frac{\text{L.V.O.} - \text{R.V.O.}}{\text{R.V.O.}} \times 100$
	kg.	l/min	l/min	l/min	Per cent
11	14.5	1.68	1.70	— 0.02	— 1.2
12	11.5	2.07	2.29	— 0.22	— 9.6
		2.26	2.50	— 0.24	— 9.6
13	25.0	3.24	2.95	0.29	9.8
		3.45	3.58	— 0.13	— 3.6
14	11.0	1.65	1.57	0.08	5.0
		2.31	2.15	0.16	7.4
16	12.0	1.03	0.99	0.04	4.0
18	8.0	0.84	0.95	— 0.11	—11.5
19	10.5	1.26	1.26	0.00	0.0
20	16.2	1.21	1.22	— 0.01	— 0.1
25	35.0	6.27	6.24	0.03	4.8
Mean		2.27	2.29	0.02	
S.D.		± 1.43	± 1.42	± 0.16	

L.V.O. = Left Ventricular Output
R.V.O. = Right Ventricular Output

Comment

The soundness of the Stewart-Hamilton indicator dilution method for estimating cardiac output has been confirmed by several workers[8-12] in the experimental studies and in comparative studies with the direct Fick principle. Usually, this procedure consists of the injection of an indicator into the venous side of the systemic circulation and the collection of blood samples from the peripheral artery, and the estimated blood flow is regarded as the output of the left heart. In order to carry out the method, the following conditions are requisite; 1) complete mixing of the indicator, 2) no escape of the indicator from the vascular compartment, 3) no regional variation in the rate of the red cells to the plasma, 4) no sequestration of blood from the general circulation, and 5) no appearance of large early recirculation of the indicator.

In the present study, these conditions requisite for estimating the right ventricular output have not been directly criticized. Instead of it, however, the right ventricular output has been compared with the left in healthy persons and in normal dogs, because of the generally accepted fact that the two outputs are equal in such cases. If both the outputs are obtained in agreement with each other in healthy persons and in normal dogs, the dilution curve drawn from the pulmonary artery may be presumed to measure precisely the right ventricular output.

The right ventricular output was in fair agreement with the left on the average, and the differences between the two outputs in individual cases were within ± 10 per cent of the right output in all except one as shown in experiment 1 and 2. These results clearly indicate that the right ventricular output can be measured reliably by this procedure, so that the present method is presumed to be applicable for detecting the difference between the true outputs of the right and left ventricles in some lung disorders. Such a reliability was also confirmed in experiment 3. Thus, the pres-

TABLE 3 — COMPARISON OF LEFT AND RIGHT VENTRICULAR OUTPUTS AND SHUNTED BLOOD FLOW IN THE DOGS WITH AN ANASTOMOSIS BETWEEN THE SUBCLAVIAN AND PULMONARY ARTERIES

Dog No.	Body Weight	L.V.O.	R.V.O.	L.V.O. — R.V.O.	Shunted Blood Flow Measured by Flow Meter	Shunted Blood Flow Measured by Bleeding Volume
	kg.	l/min	l/min	cc/min	cc/min	cc/min
16	12.0	1.95	1.83	120	110	185
17	15.0	2.63	2.26	370	480	500
19	10.5	1.40	0.99	410	480	500
20	16.2	2.08	1.52	560		530
25	35.0	5.46	5.05	410	480	340

L.V.O. = Left Ventricular Output
R.V.O. = Right Ventricular Output

ent method may be applicable for measuring bronchial blood flow to a certainty, provided that the output of the left ventricle is more than 10 per cent greater than that of the right ventricle.

In our previous studies[3,4] applying the indirect Fick principle, the bronchial blood flow was observed to be increased, sometimes 30 per cent or more of the cardiac output, in silicosis or bronchiectasis. Such a flow is sufficiently large as to be measurable by the present method. Moreover, the present method is less time-consuming and probably is more accurate than the previous indirect one, and repeated measurements are possible in any circumstance such as on exercise or at anoxia. The studies have been carried out in patients with various chronic pulmonary diseases and the results will be described in the succeeding report.[13]

SUMMARY

By measuring separately the left and right ventricular outputs using the dye dilution technique, a method for estimating bronchial blood flow was devised. In healthy persons and normal dogs, the average value of the right ventricular output was completely in agreement with the left, and differences between the two outputs in individual cases were not more than 10 per cent of the right output in all but one. It was then demonstrated that in the experimental dogs, the pulmonary collateral circulation can be measured accurately by this method. The method is considered to be preferable and reliable for estimating physiologically bronchial blood flow in man.

ACKNOWLEDGMENT: The authors wish to express their thanks to Dr. William A. Meissner and Dr. Dickinson W. Richards for invaluable suggestions on this study.

RESUMEN

Se ha ideado un método para medir el flujo sanguíneo de la arteria bronquial mediante la medida separadamente del rendimiento ventricular derecho e izquierdo por la técnica de la dilución de un colorante.

En las personas sanas y en los perros normales, el valor medio del rendimiento ventricular derecho resultó completamente de acuerdo con el izquierdo y las diferencias entre los dos rendimientos en casos individuales no fue mayor de 10 por ciento del derecho en todos, salvo en uno.

Por tanto, se demostró que en los perros que sufrieron el experimento, la circulación pulmonar colateral puede medirse con exactitud por este método. Este método se considera preferible y digno de confianza para estimar el flujo de sangre en la arteria bronquial fisiológicamente.

RESUMÉ

En mesurant séparément les débits des ventricules gauche et droit et grâce à la technique de dilution colorée, une méthode pour déterminer le débit sanguin des vaisseaux bronchiques a été définie. Chez les sujets sains et les chiens normaux, la moyenne du débit ventriculaire droit est en accord complet avec le ventricule gauche; les différences entre les deux débits dans des cas individuels ne furent pas plus de 10% du débit ventriculaire droit dans tous les cas sauf un. Il fut alors démontré que dans l'expérimentation chez les chiens, la circulation pulmonaire collatérale peut être mesurée d'une façon précise par cette méthode. La méthode est considérée comme préférable et valable pour estimer physiologiquement le débit sanguin bronchique chez l'homme.

ZUSAMMENFASSUNG

Es wurde eine Methode ersonnen zur Beurteilung des bronchialen Blutflusses durch getrennte Messung der Minutenvolume des linken und rechten Herzens unter Verwendung der Farbstoffverdünnurigsmethode. Bei gesunden Menschen und hormalen Hunden stimmte der Durchschnittswert des Minutenvolumens des rechten Herzens vollständig überein mit demjenigen des linken, und Differenzen zwischen beiden Schlagvolumina betrugen im Einzelfall nicht mehr als 10% desjenigen des rechten Herzens mit einer Auffassung vertreten, dass dieser Methode der Vorzug mitgegeben sei und dass sie zuvernale Kollateralkreislauf auf diese Weise genau gemessen werden kann. Es wird die Auffassung vertreten, dass dieser Methode der Vorzug migeben sei und dass sie zuverlässig sei zur Ermittlung der physiologischen bronchialen Zirkulation beim Menschen.

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Possibilities for Prevention of Cardiac Failure in Pulmonary Emphysema

The majority of patients with severe diffuse obstructive pulmonary emphysema develop right heart failure, and, in some cases as a later event, failure of the left heart as well. Measures which are useful in the treatment of the pulmonary disease itself are naturally of importance in the prevention of cardiac insufficiency, and this discussion could be terminated here were it not that some of the major factors which increase cardiorespiratory reserve are frequently ignored or, in one instance, misinterpreted as a hazard. It is my intention to discuss two of these factors, restoration of diaphragmatic function, and increased capacity for exercise resulting from inhalation of oxygen during a walking regimen. Ascent of the diaphragm by deliberate contraction of the abdominal musculature has been taught to patients as a breathing exercise by investigators who followed the original regimen of Hofbauer.[1] This consciously directed procedure was frequently abandoned by the patient during exertion when it was most needed. We, therefore, developed instead a training program in which the natural process of diaphragmatic respiration was encouraged by the head-down position and pressuure of the operator's hand on the patient's chest and abdomen.[2,3,4] Heckscher,[5] emphasizing the difficulty of the patient making a habit of breathing exercises that required his deliberate attention, i.e., synchronization of abdominal muscle contraction and expiration, reported remarkably favorable results from the use of the leaning forward posture to facilitate upward movement of the diaphragm. Additional aids to breathing consist of development of the diaphragmatic muscle so that no conscious effort is required to breathe against a weight of 15 to 30 pounds, applied to the abdomen and the use of an emphysema belt with an elastic recoil mechanism to increase the expiratory ascent of the diaphragm.[4] The substitution of diaphragmatic for upper costal respiration in these cases resulted in a 20 to 30 per cent decrease in pulmonary ventilation, an enhanced efficiency of exchange of both oxygen and carbon dioxide, and a decrease in energy expended as shown by decrease in O_2 consumption; a substantial dcrease in the work of the circulation and the respiration was accomplished by measures which lower the minute volume of breathing without the development of hypoxia or uncompensated respiratory acidosis.[2,3,4] Restoration of diaphragmatic function may therefore be considered a method of preventing cardiac failure in cases in which better alveolar diffusion of oxygen and carbon dioxide is produced. The value of a program of this kind depends on the degree of elastic recoil of the diaphragm which can be restored by persistent training as well as by the use of measures which decrease bronchial constriction and alveolar overdistention.

The physiologic background for the use of exercise during the inhalation of oxygen is impressive. That it has not been more widely employed

may be attributed in part to the extraordinary warnings against the continuous use of oxygen, which is recommended by some only when the patient with pulmonary emphysema and cardiac failure is ventilated by a Drinker respirator or an intermittent pressure breathing device. The fear of appropriate oxygen therapy has also been fostered by those who advocate use of air as a nebulizing agent with the intermittent pressure breathing apparatus. The hyperventilation produced by the routine use of these devices apparently may not cope with the hypoventilation induced by breathing a dilute oxygen mixture for 10 minutes' This apprehension of the marked lowering of the ventilation by oxygen inhalation and consequently relief of shortness of breath, may be contrasted to the view that hypoxia cannot be demonstrated as the cause of the dyspnea of patients with pulmonary emphysema. (Wilson et al.)[7] (Fowler et al.)[8]* In our opinion, the chemical factor in the production of dyspnea is predominantly that of hypoxia, a view recognized by many investigators. For example, Jacobs[10] states that "a natural consequence of this inability to take up and absorb oxygen in anoxia, to which all the symptoms of emphysema may be attributed." In 1938 I reported that the reduction in pulmonary ventilation in patients with pulmonary emphysema may be as much as 30 per cent in 90 seconds of inhalation of 100 per cent oxygen, with a concomitant rise in arterial oxygen saturation; at the same time a method of graduated increase of the oxygen concentration in the air breathed was described to prevent the undesirable effects of abrupt administration of high oxygen mixtures.[6] Since that time the consistent ventilatory difference between the minute volume of respiration breathing oxygen and air has been employed as a consistent test for the presence or absence of diffuse obstructive emphysema; when oxygen inhalation is properly applied, dyspnea is generally relieved by the lowered ventilation unless severe bronchospasm or fibrosis is present.[3,6]

The clinical value and the physiological results of continuous oxygen therapy have been recently reviewed in respect to restoration of cardiorespiratory compensation in pulmonary emphysema and in cardiac failure in arteriosclerotic heart disease.[4]

I shall now submit some evidence that supports the use of oxygen during exercise as a specific therapeutic procedure in the prevention of heart failure. The development of cor pulmonale was clearly related to the degree of hypoxia by Wilson et al.[7] Fowler et al.[8] and Ferer and Harvey.[12]

Ferrer and Harvey state, "The importance of bed rest cannot be overemphasized since it has already been shown that the arterial blood oxygen saturation, already low at rest, becomes much lower on exertion, and may even fall to 45 per cent in this type of emphysema subject." Rest is admittedly indicated, but oxygen therapy, in our opinion, is also important as an *early* measure and not when other measures have failed;

*Wilson et al state "Anoxia plays a minor role in the symptomatology of patients with pulmonary emphysema," and "the chief symptom is dyspnea." Nevertheless, these investigators report that oxygen administration relieves at least partially the sensation of dyspnea, and results in a marked decrease in pulmonary ventilation.

we have routinely employed continuous oxygen therapy with the regulated program mentioned without the Drinker respirator except under very rare circumstances.

The importance of rest in the acutely decompensated patient has been extended, unfortunately, to the chronic case; clinicians have indeed recognized that arterial hypoxia may be precipitated by exertion. The warnings by cardiologists of the dangers of lack of exercise in cases with coronary sclerosis and allied conditions have not appeared applicable to patients with pulmonary emphysema, largely because of the dyspnea so readily provoked as well as the trapping of air and alveolar overdistention that has been demonstrated by the maximal breathing capacity test. However, the fact that the normal person develops an increased cardiorespiratory reserve by exercise, as shown in training for athletic contests, stimulated us to try a planned exercise program while the patient inhaled oxygen; it was immediately apparent that the volume of breathing was substantially lower than when air was breathed.[2,3,4] The CO_2 was produced during the increased ventilation of exertion constituted an advantage over a similar degree of hyperventilation induced at rest since alkalotic constriction of the coronary circulation and the bronchial system was less apt to occur.

Oxygen inhalation during exercise resulted in certain specific advantages for the emphysematous patient, such as amelioration of the oxygen debt which develops during exercise with air, relief of dyspnea itself, and the decrease in minute volume of breathing.* The demonstration to the patient of an increased capacity to walk, without his accustomed breathlessness, is almost always enhanced by previous inhalation of a bronchodilator aerosol, which is, therefore, an integral part of the regimen.

The argument sometimes presented that the arterial oxygen tension is so little lowered *in these cases* as not to be a factor in their dyspnea is plainly inconsistent with the clinical response to appropriate oxygen therapy as well as inconsistent with other physiological data accumulated over a period of many years. An arterial oxygen saturation of 94 to 96 per cent, although almost normal, is nevertheless significantly low, since its elevation to normal results in relief or disappearance of dyspnea, and a train of physiological consequences including a beneficial increase in the concentration of CO_2 exhaled per breath in patients who are permitted a compensatory adjustment. IT IS BECAUSE OF THIS INCREASE IN CO_2 ELIMINATED PER UNIT VOLUME OF VENTILATION THAT THE PATIENT CAN TAKE ADVANTAGE OF OXYGEN INHALATION WITHOUT ACIDOSIS. The chemical factor in the production of dyspnea is hypoxia rather than hypercapnea. The respiratory center yields its priority to the reduction of pulmonary effort, which plainly takes precedence over the carbon dioxide stimulus; this explanation fits the re-

*There are a number of other factors which are undoubtedly involved in relief of dyspnea by an oxygen exercise regimen, i.e., pulmonary blood flow, pulmonary arterial pressure, cardiac rate and stroke volume, diffusion gradients, and perhaps oxygen enzyme systems. Darrat, Boyes and Wood,[12] reported on patients with pulmonary hypertension in which a decrease of pulmonary arterial pressure took place in 10 seconds to 2 minutes with the change from breathing air to breathing oxygen. These studies on resting individuals suggest that similar changes would occur during exertion.

sponse to therapeutic measures which increase the efficiency of alveolar ventilation better than the so-called insensitivity of the respiratory center to CO_2.[13]

Since the theory that hypercapnea is the cause of the lack of response to CO_2 in cases of pulmonary emphysema[14] must be critically modified, the rationales that was adduced in favor of routine application of mechanical hyperventilation by I.P.B. devices must be questioned for those cases well compensated to increase in arterial carbon dioxide content.

Another factor which may be responsible for reports of normal or nearly normal arterial oxygen tension in pulmonary emphysema is that patients frequently hyperventilate during the procedures involved in measuring the degree of hypoxia. I observed this phenomenon as long ago as 1920 when I drew blood from patients with respiratory and cardiac insufficiency. Although the skill in doing the procedure has increased, and pain may be absent, the observation by the conscious and at times apprehensive patient may be responsible for small increases in ventilation and consequently in alveolar and arterial oxygen tension. In two recently tested cases of convalescent coronary thrombosis, the arterial oxygen tension was increased by hyperventilation and subsequently still further by breathing 40 per cent oxygen with the pocket oxygen device, Oxy-Hale.

Case 1—Arterial pO_2 rose from 65 to 125 mm. Hg. on hyperventilation and to 170 mm. Hg. on oxygen;

Case 2—100 mm. Hg. to 135 on hyperventilation and to 230 mm. Hg. on oxygen.* The most conspicuous evidence of improvement in our cases of pulmonary emphysema exercised with oxygen was the conspicuous decreaes in pulse rate after the exercise program had been in effect for several weeks; the decreased minute volume of breathing and decreased oxygen air ventilatory difference at rest constituted the other physiological change noted later on.

In a large series now being evaluated on the effect of oxygen exercise programs a clear-cut effect could be discerned in 30 instancs but an appraisal in others was frequently impossible because patient improvement was often not based on one factor.[14] The studies of Cotes and Gilson[15] on the effect of oxygen exercise programs in 29 cases of chronic respiratory and cardiac insufficiency revealed convincing evidence of clinical improvement in 22. This investigation was well controlled in respect to the degree of tread-mill exercise and the maintenance of a similar routine program of treatment during the period when beneficial effects were observed.

W. F. Miller[16] described a remarkable case of improved respiratory function as a result of the oxygen exercise program; in his studies of patients with pulmonary emphysema the use of 50 per cent oxygen during treadmill exercise increased their exercise tolerance up to five times that tolerated on room air breathing, and also without producing as much oxygen desaturation as occurs with the shorter period of exercise with room air. Incidentally, some of Miller's patients exercised with

*These determinations were carried out by Robin W. Briehl, M.D., in the cardiorespiratory laboratory of the Presbyterian Hospital, Alfred P. Fishman, Director. They will be included in a paper, "The Ventilatory Effect of Oxygen during Exercise by Emphysematous Subjects," by Bickerman, H. A.; Nanda, H.; Beck, G., and Barach, A. L.

22 per cent oxygen and 78 per cent helium were able to double or triple their exercise tolerance with this lighter than air mixture.

Segal[17] has also reported the reduction of dyspnea with the use of 40 per cent oxygen; in one case of pulmonary emphysema the arterial oxygen saturation rose from 57 to 93 per cent after one minute of oxygen inhalations consisting of 18 inhalations from the pocket Oxy-Hale unit. Five minutes after recovery the arterial oxygen saturation was 69.2 per cent. The clinical improvement was pronounced, with disappearance of cyanosis and subsidence of dyspnea.

A fuller discussion of the effects of the oxygen exercise program will appear from our clinic but I may say in conclusion that it not only plays a clear role in physical rehabilitation but makes possible excursions for those human beings into the outside world that in themselves may add profoundly to their well being; respiratory function tests do not record feelings of optimism nor the satisfaction obtained from the recognition of progress. Patients with pulmonary emphysema appreciate the increasing use of oxygen inhalation during exercise at home and out of doors although the practitioners' fear of over-publicized oxygen toxicity is a problem that has to be coped with by explaining that fears of the appropriate, well regulated use of oxygen therapy are groundless. I have recently attempted to provide some simple methods by which the patient may employ ambulatory oxygen therapy.[18] Reification of the chemical concept of dyspnea in the writer's opinion will lead to increasing acceptance of the predominating etiological role of oxygen-want in the symptomatology of pulmonary emphysema.

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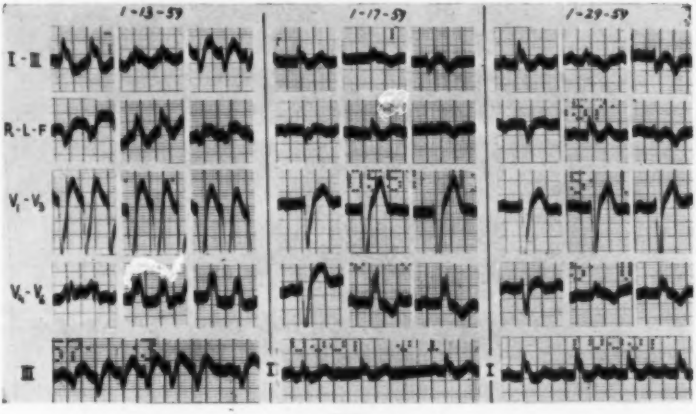
ELECTROCARDIOGRAM OF THE MONTH

Recent Posterior Wall Infarction in the Presence of Left Bundle Branch Block, with Pseudo-Ventricular Tachycardia and Pseudo-Preexcitation

A 72 year-old woman was admitted to Michael Reese Hospital for sudden chest pain, incipient pulmonary edema and gallop rhythm; her blood pressure was 150/100. She responded well to digitalization, morphine and oxygen therapy and was discharged after an uneventful hospital course. Her electrocardiograms are instructive from three aspects.

1) Pseudo-ventricular tachycardia: In the tracing of January 13, 1959, the day of admission, the rapid and uneven ventricular action (average rate 150), associated with slurred and widened QRS complexes, suggests a paroxysmal tachycardia of ventricular origin. However, the true nature of the rhythm is revealed by studying the intermittent irregularity (lowest strip). A group of fast beats, with at first shorter and shorter R-R intervals, is followed by a pause measuring less than twice the duration of the short R-R intervals. This is the structure of the ventricular arrhythmia caused by a Wenckebach period. The first beats initiating the fast run, and terminating the pause, are preceded by a P wave of normal contour (not discernible elsewhere) at a P-R interval of 0.20 sec. On this basis, a ventricular tachycardia can be excluded and the impulse located as originating in the sinus node. Transmission of the fast sinus impulses to the ventricles is impaired by a second degree A-V block and by the presence of a left bundle branch block.

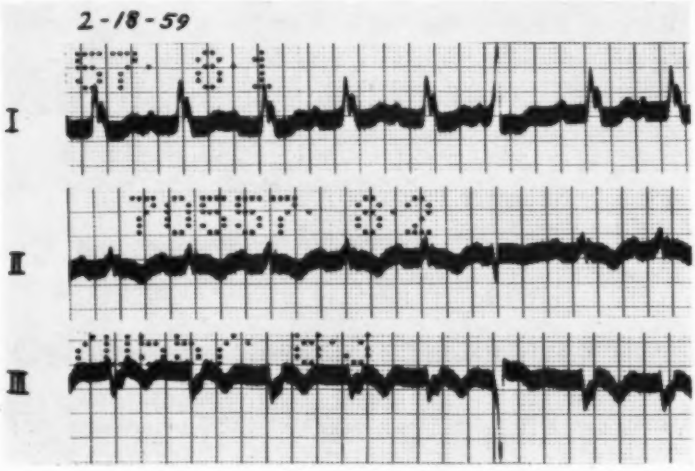
2) Recent posterior infarction in L.B.B.B.: On January 17, 1959 the sinus rate has slowed to 88 and both a second degree A-V block and a left bundle branch block are still present. The former is revealed in the lowest strip where a ventricular beat is dropped subsequent to P-R prolongation from 0.20 to 0.34 sec.; the latter is demonstrated by the QRS prolongation to 0.14 sec. and by the typical configuration of the precordial leads. However, the limb leads fail to show the characteristic contour in



that S-T is depressed and T upright in leads I and aVL, whereas S-T is elevated and coved and T symmetrically inverted in leads II, III and aVF. These are features characteristic of a recent posterior wall infarction, a diagnosis supported by the evolution seen in the record of January 1, 1959, 12 days later. While the A-V block has regressed to a first degree, the S-T deviations have disappeared and the T waves are more upright in leads I and aVL and more inverted in leads II, III and aVF, characteristic for a subacute stage of posterior wall infarction. It is usually difficult or even impossible to recognize a recent myocardial infarct in the electrocardiogram when a left bundle branch block is present. The characteristic QRS and ST-T alterations of infarction are obscured by the abnormal order of left ventricular activation and deactivation. In this instance, although typical QRS changes failed to develop, the diagnosis could be entertained, since primary ST-T alterations with a characteristic evolution, caused by injury and ischemia, outbalanced the secondary ST-T changes consequent to the abnormal ventricular activation in the limb leads; moreover, the diagnosis was supported by the transient appearance of an A-V conduction disturbance, a common occurrence in early stages of posterior wall infarction.

3) Pseudo pre-excitation (WPW): The record of February 18, 1959 shows an isolated ventricular complex with typical earmarks of ventricular preexcitation (WPW) in each of the three standard leads, suggesting that on occasion the sinus impulse reaches the ventricles over two pathways: i.e., the normal one and an accessory abnormal A-V connection remote from, and thus avoiding, the conduction obstacle in the A-V node. However, two objections oppose such a simple interpretation:

a) The interval from the beginning of P to the *end* of the QRS of the anomalous beats (0.22 sec.) is shorter than the P-R interval (0.26 sec.) in the dominant beats. This implies that ventricular activation is completed before the arrival of an excitation front passing down the ordinary A-V junction.



b) The QRS duration of the anomalous beats (0.12 sec.) is shorter than that of the dominant beats (0.14 sec.). This implies that in the former beats, ventricular activation starts in a more central area of the ventricular septum, below the blocking lesion in the left bundle branch which is responsible for the more marked QRS prolongation in the dominant beats. Two other possible interpretations remain: a) that ventricular activation of the anomalous beats is effected entirely via a preexcitation path which terminates within the ventricular septum; or b) that there is no accessory (preexcitation) connection between the atria and ventricles, the anomalous beats being caused by occasional premature ectopic impulses arising within the septum, independent of, and interfering with, the preceding sinus impulse. The sporadic occurrence of the beats under question, as well as present knowledge concerning prexcitation mechanisms favors the last interpretation.

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The Committee on Electrocardiography and Vectorcardiography welcomes comments. We would also be pleased to receive EKG's of exceptional interest with brief history. Please submit material to: Stephen R. Elek, M.D., chairman, 6423 Wilshire Boulevard, Los Angeles 48, California.

X-RAY FILM OF THE MONTH

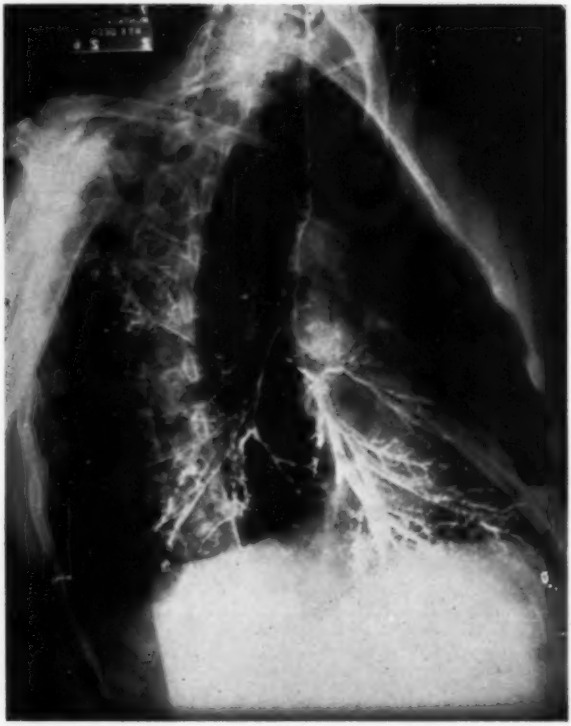
Clinical Information

A 55 year-old white male. Shortness of breath, slight cough. Physical examination normal. Electrocardiogram normal. Laboratory studies normal.

Answer: SUPERNUMERARY TRACHEAL LOBE

The supernumerary lobe is one of the rarest anomalies of the chest. However, more and more cases have been reported with the recent advances in thoracic surgery and the increased use of the bronchoscope and bronchography. The tracheal bronchus is seen in many mammals, such as the pig and sheep, but in man, this is an anomaly. According to Foster-Carter, the following nomeclature is used: if one of the segments or subsegments of the right upper lobe, usually the apical segment, is displaced onto the trachea, this is called a displaced bronchus. If the right upper lobe has all normal lobar segments, the tracheal lobe is called a supernumerary bronchus. The displaced bronchus is seen more often than the supernumerary bronchus, which is believed to be quite rare.

In the following case, the supernumerary bronchus arose three cen-



timeters above the main carina, posteriorly on the right side. The orifice of this lobe could be visualized with the right angle scope and would be easily missed if the trachea were not examined thoroughly with the right angle scope. All three orifices of the right upper lobe were well-visualized by the right angle scope and these segments can be seen easily in the bronchogram.

The tracheal lobe is not just of academic interest, as it has considerable importance to the thoracic surgeon in lobectomy and segmental resection. Occasionally, it is the source of bronchiectasis and other pathological changes. Epstein reported a case of bronchial adenoma in a supernumerary lobe and Holinger reported a case showing accessory tracheal bronchus leading to a congenital cyst. It is felt by the writer that this anomaly will be picked up more frequently with more diligent use of the right angle scope in bronchoscopic examinations.

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The Committee on Chest Roentgenology welcomes comments. We would also be pleased to receive x-ray films of exceptional interest with a brief history. Please submit material to: Benjamin Felson, M.D., Department of Radiology, Cincinnati General Hospital, Cincinnati, Ohio.

Fibroma of the Heart

CASE REPORT

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GABRIEL SANCHEZ, M.D., F.C.C.P., FIDEL AGUIRRE, M.D.,
JULIO JUNCO, M.D. and ALBERTO GARCÍA PALACIO, M.D.*
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Although primary tumors of the heart are of rare occurrence in children, it is important to bear them in mind, for they can be mistaken for congenital heart malformation. With the increasing progress in open heart surgery, the diagnosis during life is of paramount importance. The majority of primary heart tumors are benign. The most frequent are the myxomas, followed by fibromas, rhabdomyomas, hamartomas, lymphangiomas, teratomas, lipomas and cysts.

There have been only four proven primary malignant tumors of the heart reported in the medical literature. Bigelow[1] reviewed eight cases of heart fibromas and added one. McCue[2] reported another case. We believe this is the first report of a primary fibroma of the heart in an infant in our country.

Case Report

D. F., a colored girl, eight months old, was admitted to the Pediatric Service, "Nuestra Sra. de las Mercedes" Hospital, May 26, 1955, with shortness of breath. Present illness: the mother states that in the past two months the child had four spells of coldness, paleness, profuse sweating and crying. A week prior to admission, she was seen in another hospital for shortness of breath and slight temperature (37.4° C.) An x-ray film of the chest then showed an enlarged heart. Past history: Chicken-pox at the age of six months, and repeated bouts of bronchitis for two months. Psychomotor development: slightly retarded. Physical examination: Well developed (68 cms.), slightly undernourished (15.5 pounds), non-cyanotic girl. The thorax: There was

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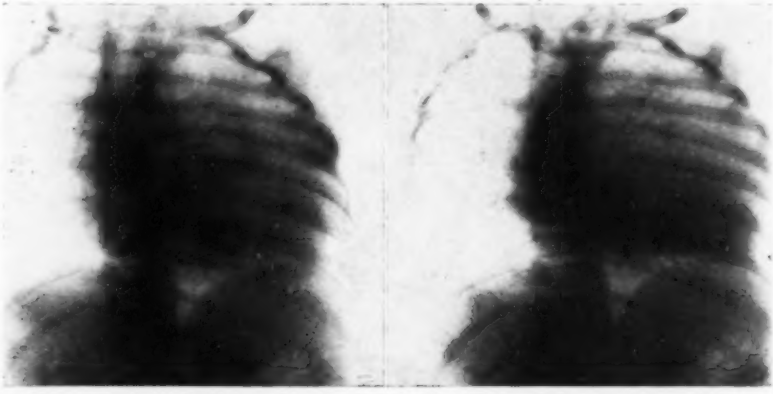

FIGURE 1: Telecardiogram: Cardiomegaly with left ventricular hypertrophy.

FIGURE 2: Angiocardiogram: The left ventricle somewhat deformed perhaps resembling a filling defect.

slight elevation of the precordium, with visible apical heart beat on the 5th and 6th left interspaces and palpable on the fifth interspace and mid-clavicular line. Tachycardia, 120 pulsations per minute. A systolic murmur grade II was audible at the base area. Palpable femoral pulses. Blood pressure: Upper limbs, 88 mms. Hg. systolic, 50 mms. Hg. diastolic; lower limbs, 100 mms. Hg. systolic, 60 mms. Hg. diastolic. Forty four respirations per minute. Dullness on percussion of the mid right posterior hemithorax and bronchophony in the same area. The abdomen: the lower border of the liver palpable 2.5 cms. below the costal margin. The results of laboratory examinations were as follows: Blood count: 4.5 millions red cells, 11.5 grs. hemoglobin, 15.000 leucocytes, 1 per cent juvenils, 47 per cent neutrophils, 42 per cent lymphocytes, 6 per cent monocytes, 3 per cent eosinophils. Eritrosedimentation rate: 40-98 Westergreen. Urea nitrogen: 24.14 mgs. per cent, blood sugar: 80 mgs. per cent, Kahn and Meinicke negative. Negative tuberculin test, urine and stool analysis. Telecardiogram: enlarged heart, left ventricular hypertrophy (Fig. 1). The electrocardiogram revealed tachycardia 166 per mn. negative T waves in D1, diphasic in D2, positive in D3. Sharp morphologic change of QRS from V2 to V3. T wave positive in V1 and V2, negative from V3 to V6; QRS pattern from V4 to V6 with tall R waves. Left ventricular hypertrophy with strain. Hospital course: Five days after admission her general condition and bronchitis had improved, she had received thiamine, B complex, vitamin C and aureomycin. Ten days later, she had another bout of bronchitis and improved again under the above treatment. A month after admission, she had coldness, sweating and restlessness. Next day she showed marked dyspnea and cyanosis. Absent breath sounds over the posterior mid-hemithorax and bronchophony over the upper half of the right side of the chest. Her pulse was countless. She was digitalized intravenously and sedated. An electrocardiogram showed myocardial ischemia, left ventricular hypertrophy and supraventricular paroxystic tachycardia. She improved some under digitalis, but the paleness, coldness, profuse sweating and crying became more frequent. An angiocardiogram (Fig. 2) showed heart enlargement, but was not diagnostic. A muscle biopsy for glycogen storage disease was also negative. By elimination, the diagnosis of endocardial fibroelastosis was established. A Beck I operation was decided upon and performed on August 26, 1955. Under sodium penthotal, she was intubated endotrachealy and pure oxygen was used. While making the incision on the left thorax, little bleeding was noticed from there on. The anesthesist reported absence of pulse

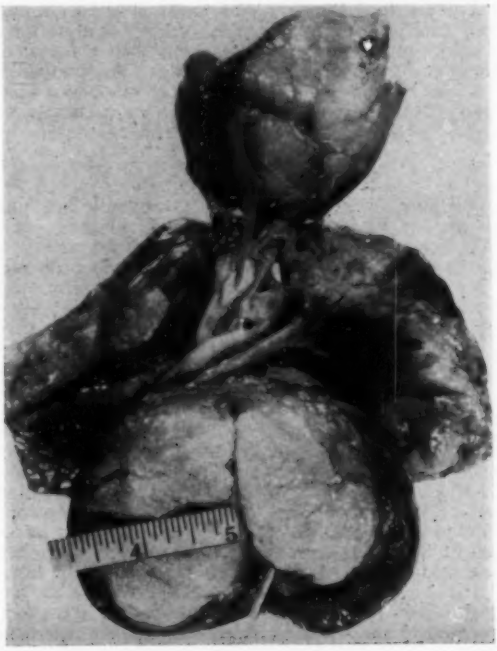

FIGURE 3: The main mass of the tumor occuping the interventricular septum.

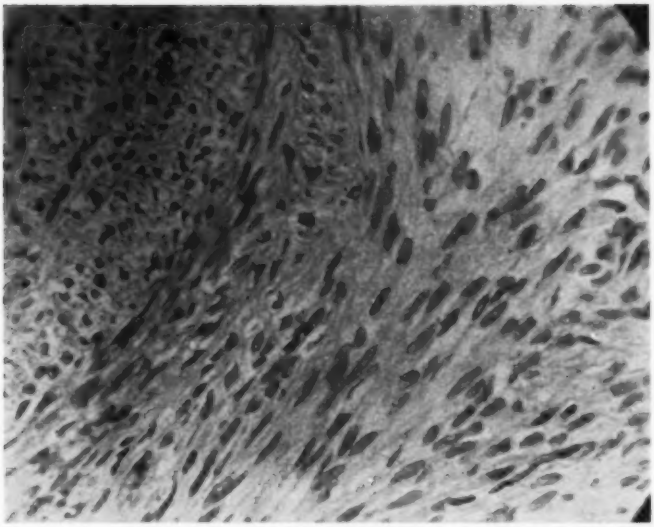

FIGURE 4: High power view showing the fibroblastic elements which constitute the fibroma.

and blood pressure. Immediately the thorax was entered and cardiac massage started. This was continued for 90 minutes when the diagnosis of irreversible cardiac arrest was established. At necropsy the heart was enlarged, especially the left ventricle. On opening the heart, there was a 7 cms. in diameter white-greyish rounded tumor mass (Fig. 3) arising from the ventricular septum, extending to the wall of the left ventricle and protruding into the left ventricular chamber producing a true sub-aortic stenosis. Macroscopically the tumor was identical to a uterine fibroma. No other cardiac anomaly was present. Aside from a slight liver congestion, the rest of the necropsy was negative. Microscopic studies revealed the fibroblastic nature of the tumor (Fig. 4). It was almost entirely composed of fibroblasts and fibrocytes mixed with collagen fibers. This tumor was fairly well encapsulated, although in certain areas cardiac myofibrills could be seen crossing those of the tumor.

Discussion

The diagnosis of heart tumor during life is difficult, but has been made on several occasions. In our case which had paleness, coldness, sweating and crying, we thought of the possibility of an anomalous coronary artery, arising from the pulmonary artery. The clinical course and the electrocardiogram ruled this out. Acute beri-beri was also ruled out by the absence of neurologic signs and the lack of response to the massive administration of vitamin B_1. Glycogen storage heart disease was ruled out by muscle biopsy. By elimination and with the positive findings of cardiomegaly with left ventricular hypertrophy and a murmur of low intensity, the diagnosis of endocardial fibroelastosis was clinically established. With this diagnosis in mind and trying to revascularize the heart, the Beck I operation was recommended. Looking back, perhaps the correct diagnosis could have been established from the angiocardiograms (Fig. 2). On the films the right side cavities seem somewhat displaced from left to right, and the right ventricle is not well outlined. The right ventricle outflow tract and pulmonary artery seem somewhat elevated. On the late films (Fig. 2) the left ventricle seems somewhat deformed losing its ovoid shape, perhaps resembling a filling defect. On the other hand, the tumor arising from the septum and protruding within the left ventricular cavity, acting as a sub-aortic stenosis, could well explain the coronary symptoms. According to medical literature, the most frequent location of primary fibromas of the heart is the left ventricle.[3-7] Next to this location is the interventricular septum[8] followed by the auricles.[9] Bigelow[1] established the differential diagnosis between fibromas and rhabdomyomas. He believes that rhabdomyomas are not true neoplasms. The so-called fibromas are much like the uterine leiomyomas while rhabomyomas resemble hemartomas. True fibromas have been reported under the name of rhabdomyoma,[4] fibrosarcoma[5] and hamartoma.[6]

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Bilateral Simultaneous Spontaneous Pneumothorax

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Bilateral simultaneous spontaneous pneumothorax, although rare, may constitute a grave emergency when it does occur. Early diagnosis and institution of prompt therapeutic measures may be essential for survival. The great majority of cases of spontaneous pneumothorax involve one lung only and are readily treated by simple aspiration of the air, or by intercostal catheter and water seal drainage. In general, thoracotomy is reserved for those cases which may be classified as chronic or recurrent pneumothorax. On the other hand, a recent experience with a case of bilateral simultaneous pneumothorax has demonstrated that in such a circumstance, early thoracotomy is justified and desirable in order to avoid a subsequent and possibly fatal recurrence.

Case Report

P. C., a 22 year-old white man was admitted to The George Washington University Hospital on November 18, 1958 having been transferred from another hospital out of town. Six months previously, he awoke one morning with dull, substernal pain and dyspnea. He was taken to a local hospital where a roentgenogram of the chest showed bilateral pneumothorax. This was treated by aspiration and he was discharged from the hospital after 18 days. He was well in the interim until November 12, 1958. At that time, he again awoke with severe right anterior chest pain which was aggravated by inspiration. He developed progressive dyspnea and his mother noted that he was cyanotic and disoriented. He was readmitted to the local hospital where immediate aspiration of air was carried out after a roentgenogram had again demonstrated bilateral pneumothorax (Fig. 1). A chest tube was inserted and his condition improved. He was subsequently transferred to The George Washington University Hospital. At the time of admission, physical examination showed a thin, white man in no distress. Temperature was 37.2° centigrade; pulse 94; blood pressure 130/75. The head and neck were not remarkable. Examination of the chest revealed diminished breath sounds throughout both sides of the chest, more marked on the left. There was diminution in vocal and tactile fremitus and a few fine rhonchi were present bilaterally. The remainder of the examination was within normal limits.

Laboratory Data: Hematocrit 46; WBC 13,300 ; Seg. 71; Bands 12; Lymphocytes 17; Urinalysis normal; V.D.R.L. negative; Blood type B+. Chest x-ray film on the day of admission showed 30 per cent pneumothorax on the left and a 25 per cent on the right. Small amounts of fluid were present in both pleural cavities.

Course in the hospital: On November 21, 1958 bilateral anterior thoracotomy was performed under general endotracheal anesthesia. Since no intercostal catheters had been inserted, the chest was entered rather rapidly to avoid the development of tension pneumothorax. Incisions were made in both submammary regions extending from the lateral border of the sternum on each side to the axilla. The chest was entered on each side through the fourth intercostal space. Upon entering the pleural spaces, the left lung was found to be approximately 30 per cent and the right lung approximately 40 per cent collapsed. The lungs were immediately expanded. It was noted that the visceral and parietal pleurae were considerably injected, particularly on the left side. There was a small area of scarring at the apex of the left lung with a residual emphysematous bleb approximately two centimeters in diameter at the apex of the left lung. There was a small scarred area at the apex of the right lung, but no definite bleb could be demonstrated. There was no evidence of an air-leak or bronchopleural fistula at this time. The bleb at the apex of the left lung was then resected. The visceral and parietal surfaces of both pleural spaces were then lightly abraded with a dry gauze sponge and powdered with sterile USP talc. Chest catheters were then inserted in the second interspace in the anterior axillary line and the eighth interspace in the posterior axillary line bilaterally. The wounds were then closed in layers in routine fashion. A postoperative roentgenogram of the chest demonstrated full expansion of both lungs.

Postoperatively, there was no evidence of air-leak from either pleural space. There was a small amount of serosanguineous drainage from both pleural cavities for the first 48 hours postoperatively. All chest tubes were removed on the third postoperative

From the Department of Surgery, The George Washington University School of Medicine.

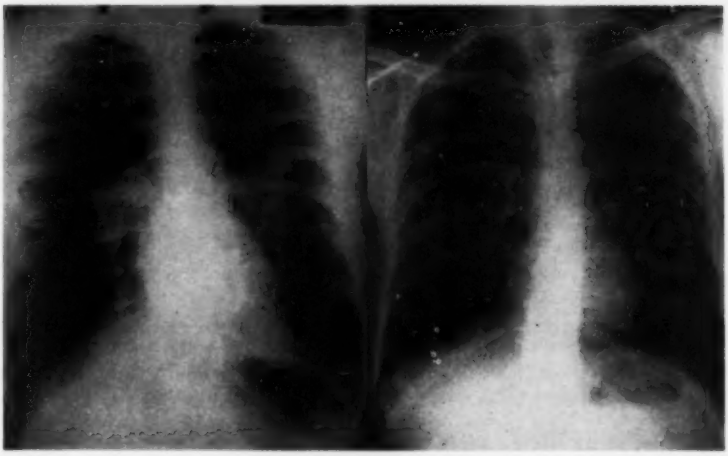

FIGURE 1: Chest roentgenogram demonstrating simultaneous bilateral pneumothorax (see text). FIGURE 2: Chest roentgenogram of same patient taken six weeks postoperatively.

day. The remainder of the convalescence was not remarkable except for a superficial wound infection in the right thoracotomy incision. This was treated with irrigation and daily dressings and healed satisfactorily. His lungs remained fully expanded and he was discharged from the hospital on his 22nd postoperative day and returned home.

He was last seen on January 9, 1959 as an out-patient. At that time he was asymptomatic, the wounds were well healed and both lungs were fully expanded (Fig. 2).

Discussion

It has been our policy to advise thoracotomy in those patients who have had a recurrent spontaneous pneumothorax or in those cases where a persistent air-leak exists after four to five days of treatment with water seal drainage. At the time of operation any blebs which may be present are resected and the surface of the lung is powdered with USP talc. This serves to create adhesions between the visceral and parietal pleura and prevents any subsequent development of pneumothorax.[1,2]

It would appear, however, that in the event of bilateral simultaneous spontaneous pneumothorax, one should be somewhat more aggressive in the surgical approach. At the time of the initial episode, once the lungs have been expanded either by aspiration or water seal drainage, early elective thoracotomy should be carried out. It would seem unwise in this situation to wait for a recurrence, since this could possibly occur in a location where the patient would be unable to obtain immediate medical care and the result could easily be fatal. It is apparent that the immediate treatment instituted at the time of the second episode in the case described was life-saving. If this episode had occurred under circumstances where immediate care was not available, the patient probably would not have survived.

Bilateral simultaneous thoracotomy has gained popularity in recent years, especially in operations on the heart and great vessels. This approach has also been advocated for simultaneous bilateral pulmonary resection,[3,4] and Baronofsky has advocated bilateral thoracotomy in the treatment of unilateral pneumothorax and pulmonary blebs.[5] It is our opinion that simultaneous bilateral thoracotomy is rarely necessary for pulmonary disease. We do not agree with Baronofsky's concept of routine bilateral thoracotomies in the treatment of unilateral pneumothorax. In patients with bilateral pulmonary blebs, with or without associated pneumothorax, when bilateral operations are indicated, it has been our practice to operate on one side at a time. Under such circumstances we believe that these operations should be performed in two stages at intervals of three weeks or more.

On the other hand, in a patient with bilateral simultaneous pneumothorax, simultaneous bilateral operation would appear to be advisable. The possibility of recurrent contralateral pneumothorax in the postoperative period following thoracotomy on one side would appear to be great. A case similar to the one reported herein has been recorded by Reeves et al.[6] We disagree slightly with these authors in that we do not believe that bilateral thoracotomy for this condition requires transection of the ster-

num. In addition, we believe that talc poudrage is of great benefit in the prevention of further episodes of pneumothorax. The use of talc does not appear to increase the postoperative pain or morbidity and is certainly more simple and less dangerous than pleurectomy, as advocated by some authors.[5,7,8] Talc poudrage does not reduce subsequent pulmonary function.[9]

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Editorial

The Use of Audiovisual Aids in Teaching

The significance of the visual image in mental processes received important recognition in the old Chinese proverb that one picture is worth ten thousand words. That proverb was exploited in the great teaching programs developed by the armed forces during World War II when much unfamiliar factual information and many technical procedures had to be rapidly assimilated by millions of men. Efforts in utilizing this technique in medical teaching programs have been sporadic and highly individual; in some institutions that have recognized its importance, film lists, and siled and film libraries have been assembled, while other undergraduate and postgraduate programs are entirely devoid of anything but the simplest, most obsolete use of this teaching medium.

Visual and audiovisual educational techniques are highly developed. In using the medium, a number of points must be considered: (1) The quality of the material to be used; (2) Its appropriateness to the subject and to the group to whom it is to be shown; (3) The availability of the material and the facilities required for its use; (4) Finally, the manner in which the material is to be used. This requires planning and integration.

Much of the medical audiovisual material prepared today for distribution is in the form of motion or still pictures that totally cover a given subject. This may consist of a broad coverage of a general subject, or a thorough, detailed analysis and presentation of a specific problem. Such coverage tends to be lengthy and to substitute rather than augment a presentation that an instructor might wish to make. Short film strips such as were prepared some years ago by the audiovisual committee of the Association of American Medical Colleges represents material that illustrates the lecturer's presentation rather than displaces it. Each way of using this teaching medium has its place and the material, subject and manner of presentation must be correlated for most effective response.

The number of good teaching films for undergraduate, graduate, hospital, nurse, and lay groups is great. Many organizations prepare approved lists of films dealing with every phase of medicine. The recent list published by the American College of Chest Physicians covers the basic subjects of anatomy, physiology, embryology and pathology of the cardiorespiratory and upper gastrointestinal systems. More voluminous are the films listed on diagnosis and treatment of the diseases of the chest. Those films suitable for undergraduate teaching are so indicated in the approved film list. Similar lists are prepared by the American Medical Association, the American College of Surgeons, the Association of American Medical Colleges and others. Titles, authors, content, running time and place of procurement of films are given in the film lists. The authors are desirous of having the films used and therefore arrangements for procuring them are always simple.

PAUL H. HOLINGER, M.D., F.C.C.P.
Chicago, Illinois

DR. ARTHUR M. MASTER

DR. ARTHUR M. MASTER

RECEIVES 1960 COLLEGE MEDAL

Dr. Arthur M. Master, New York City, was presented the College Medal for meritorious achievement in the field of cardiovascular diseases at the annual meeting of the College in Miami Beach on June 11, 1960. The award was made by Dr. Andrew L. Banyai at the Presidents' Banquet held at the Saxony Hotel.

Dr. Master was born on December 1, 1895 and received his pre-medical education at the College of the City of New York, graduating with the degree, Bachelor of Science, in 1916. Dr. Master graduated in 1921 from Cornell University Medical College, interned at the Mount Sinai Hospital and served as Admitting Physician there. He was awarded the Cornell University Medical College Travelling Fellowship and worked with Sir Thomas Lewis at the University College Hospital Medical School, London, England, in 1924 and 1925.

Dr. Master served in the Navy in World War I, and in World War II as a Captain. During World War II, he was Cardiologist of the National Naval Medical Center at Bethesda, Maryland, Chief of Medicine at the U. S. Mobile Hospital in the Solomon Islands, and Consulting Cardiologist at the Aeia Heights Hospital, Honolulu. He is author of more than 300 articles on cardiovascular diseases and internal medicine. His special interests have been coronary occlusion, acute coronary insufficiency without occlusion, new definitions of "ideal," "average" and elevated blood pressure, the "2-step Master" exercise test, chest pain, blood pressure, height and weight in the aged, the electrocardiogram in acute diseases, etc. He has written three books, ***The Electrocardiogram and X-ray Configuration of the Heart, Cardiac Emergencies and Heart Failure, and Normal Blood Pressure and Hypertension: New Definitions.***

Dr. Master is now the Consultant Cardiologist of the Mount Sinai Hospital, New York City, Englewood Hospital, Engelwood, New Jersey, the U. S. Public Health Service Hospital, Staten Island and has served as cardiologist or consultant cardiologist of many hospitals, including St. Alban's Naval Hospital and Gouverneur Hospital.

He is an Associate Editor of the ***New York State Journal of Medicine, The New Physician, GP, Excerpta Medica*** (both cardiovascular diseases and chest diseases), and ***Diseases of the Chest.*** He is also Chairman of the Committee of Special Subjects, New York Academy of Medicine, Member of the Executive Committee, New York Heart Association, and Past President of the New York County Medical Society.

Among the numerous societies in which Dr. Master holds membership are the American Medical Association, American Heart Association, American College of Physicians and American College of Chest Physicians.

The President's Page

THE DOCTOR AS A WHOLE MAN

One of the most pleasant prerogatives attached to the Presidency of the American College of Chest Physicians has been the traditional access to the editorial pages of *Diseases of the Chest*. As physicians, we all have ample opportunity to publish the results of our research on particular medical problems. But one seldom has an opportunity to speak his mind on the larger professional concerns. One seldom has an opportunity to talk about medicine in a general way, or about the doctor's relationship to medicine, or about his non-medical responsibilities. Access to the editorial pages of this journal is such an opportunity, and it would have been only fair to warn readers that we proposed to take full advantage of it during the past year.

What we had to say was couched in moderate terms. There was no reason to sound the tocsin; indeed, there is good cause for rejoicing. At no time in history has medical progress been so spectacular as in the first half of the twentieth century. As regards the availability of accurate medical knowledge, this is of course a truism. Not so obvious but perhaps equally significant has been our success in establishing standards of professional competence. The doctorate in medicine implies today a very high degree of knowledge and ability. One has only to thumb through the Flexner Report of a half a century ago to see how much of an achievement this has been.

But progress is not automatic. Our own fortunate situation is in large measure an inheritance; the good things of the present we owe to the foresight and the will of our predecessors. And we are obligated to exercise the same qualities for those who will come after.

Nor is the present situation without its disturbing portents. Some writers describe the whole society as meaningless for most of the individuals in it because of the fragmentation of their activities. Work, they say, is performed with no object in view but wages, and wages are spent to make the time pass. Communities exist without a community of interests, family relationships are superficial, and so forth. We do not pretend to pass on the validity of these charges so far as society at large is concerned, but certainly the possibility of such fragmentation is everywhere visible in medicine today. Specialization with its advantages and disadvantages is only the most obvious threat to the wholeness of a doctor's life. Other forces would seem to be working to the same end. There is surely at least an impulse abroad in some public circles to regard medicine as a business, to turn it into an eight to five affair, to regard it as a necessary if boring means to the good life around the swimming pool and the barbecue pit. But this is to make the practice of medicine as meaningless as plastering radiator ornaments on cars on an assembly line.

And the very abundance of new information available each year brings with it certain hazards. Everyone would agree that there is a difference between the well-informed doctor and the wise one. Wisdom implies a wholeness of knowledge, a sense of proportion. Obviously the presses groaning with medical publications are an invitation to intellectual indigestion. How can we learn to assimilate the riches that research offers us? Perhaps an even more fundamental question is this: will not the generation of doctors now in medical schools be in a more difficult position than the present generation? How can one train a doctor to keep abreast of current developments without sacrificing understanding?

These are real problems, and our obligation to consider them is also real. The future is not necessarily the result of impersonal forces operating in the present; the foresight and the will which we exercise today can also have their effect. We have hoped that the use of these columns has stimulated such foresight and will.

Seymour M. Farber

DISEASES *of the* CHEST

VOLUME XXXVII

JANUARY-JUNE, 1960

DISEASES *of the* CHEST

OFFICIAL PUBLICATION

OF THE

AMERICAN COLLEGE OF CHEST PHYSICIANS

EXECUTIVE OFFICE
112 East Chestnut Street, Chicago 11, Illinois, U.S.A.

MURRAY KORNFELD, *Managing Editor*

WARD BENTLEY, *Publication Manager*

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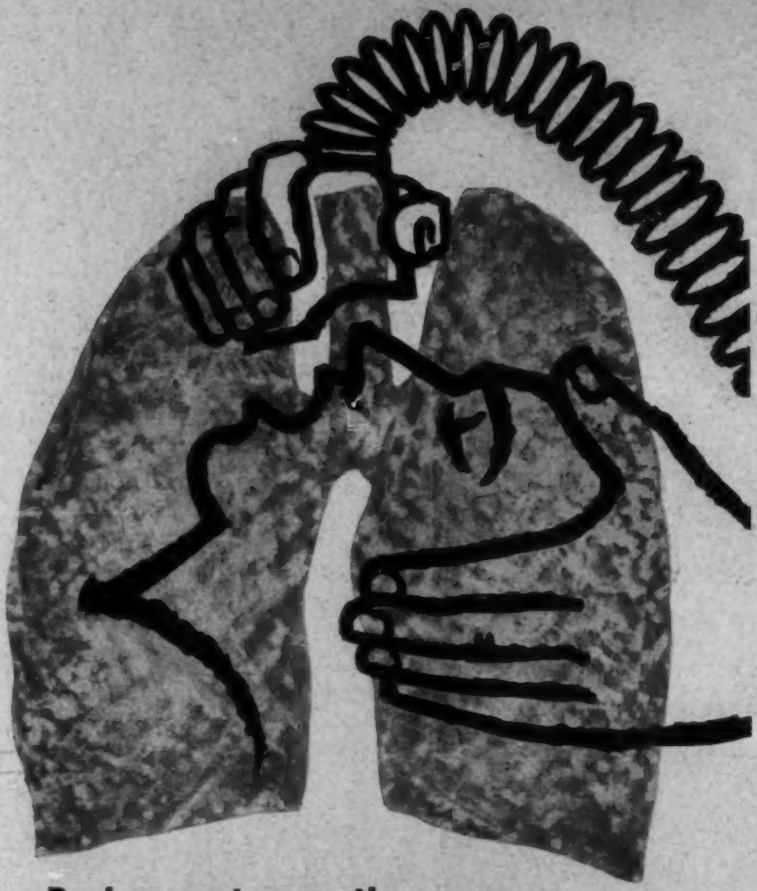

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